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OFFICE OF PREVENTION,  
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MEMORANDUM

SUBJECT: EFED Revised Registration Review Problem Formulation for Tralomethrin

FROM: José L. Meléndez, Chemist  
Amanda Solliday, Biologist  
Environmental Risk Branch V  
Environmental Fate and Effects Division (7507P)

*Jose Luis Melendez*  
*Amanda A. Solliday* 3/23/10

THROUGH: Mah T. Shamim, Branch Chief  
Environmental Risk Branch V  
Environmental Fate and Effects Division (7507P)

*Allen W. Veen*  
03/23/10

TO: Joy Schnackenberg, Risk Manager Reviewer  
Robert McNally, Risk Manager  
Risk Management and Implementation Branch IV  
Pesticide Re-Evaluation Division (7508P)

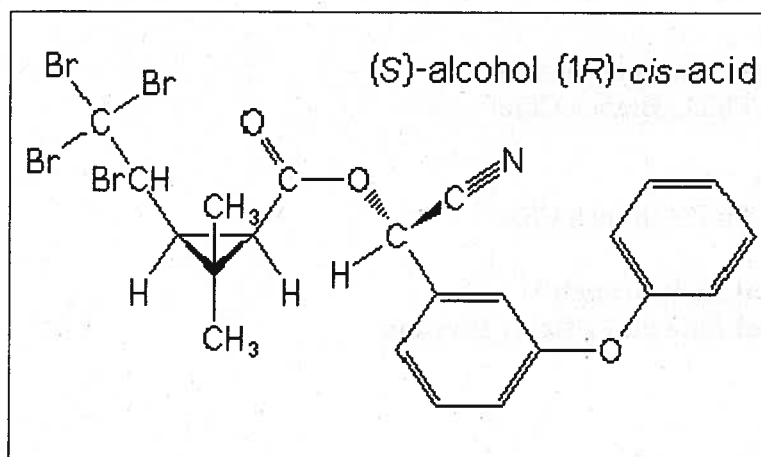
EFED has revised the ecological risk assessment problem formulation for tralomethrin registration review (attached).

Changes from the original problem formulation (DP 365550, 12/15/09) include:

1. The deltamethrin registration review problem formulation (DP 373622) is referenced in the "Nature of the Regulatory Action" section, as deltamethrin is a major degradate of tralomethrin and a registered active ingredient.
2. A more clear explanation of Agency knowledge of the degradation of tralomethrin to deltamethrin was added to "Stressor Source and Distribution" and "Environmental Fate & Transport" sections.
3. Biomagnification potential is now included in Table 3.1.
4. Interactions with the potentiators piperonyl butoxide and MGK are addressed in "Overview of Pesticide Usage".

5. A statement discussing tralomethrin metabolism in rats was added in "Aquatic and Terrestrial Effects".
6. In the effects data gaps section, the need for estuarine/marine aquatic toxicity studies was linked to current use patterns that include coastal areas. The effects data gaps section now also includes a description of TEP testing requirements and the need for these TEP estuarine/marine acute toxicity studies based on aquatic EECs reported in previous tralomethrin assessments. These changes are also reflected in the Appendix A data justification tables.
7. The data requirements for the degradate deltamethrin are included.

# Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review of Tralomethrin



March 23, 2010

Environmental Fate and Effects Division  
Office of Pesticide Programs  
US Environmental Protection Agency



**Prepared by:**

Amanda Solliday, Biologist  
José L. Meléndez, Chemist

**Reviewed by:**

Keith Sappington, Senior Scientist  
Mah Shamim, Ph.D., Branch Chief

**Approved by:**

Mah Shamim, Ph.D., Branch Chief

**Environmental Risk Branch V**  
**Environmental Fate and Effects Division**

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## **1. Purpose**

The purpose of this problem formulation is to provide the foundation for the ecological risk assessment being conducted for the registered uses of tralomethrin. As such, it articulates the purpose and objectives of the risk assessment, evaluates the nature of the problem, and provides a plan for analyzing the data and characterizing the ecological risk (EPA, 1998). Additionally, this problem formulation is intended to identify data gaps, uncertainties and potential assumptions needed to address those uncertainties in characterizing the ecological risk associated with the registered uses of tralomethrin.

Tralomethrin is a synthetic pyrethroid insecticide that is registered for a variety of agricultural and residential uses, including (but not limited to) broccoli, cotton, lettuce, soybeans, sunflowers, household/ domestic dwellings, ornamental and/or shade trees, ornamental ground cover, ornamental herbaceous plants, lawns and turf, pet living/sleeping quarters, garbage cans, paths/patios, and wood protection treatment, industrial areas outdoor, non-agricultural outdoor buildings/ structures, ornamental lawn, turf, non-flowering plants, woody shrubs and vines, paved areas (roads/ sidewalks, solid waste sites, agricultural farm premises (indoor), autos, recreational vehicles, ships, boats, caskets, warehouse premises and equipment (indoors and outdoors), eating establishments, egg packing plants, food processing plants and premises, food stores, grain products (processed), greenhouses, hospital/ medical institutions, household/ domestic dwellings, meat processing plants, poultry processing plant premises and public buildings/ structures.

## **2. Problem Formulation**

### **2.1. Nature of Regulatory Action**

The Food Quality Protection Act of 1996 mandated the EPA to implement a new program, *i.e.*, registration review ([http://www.epa.gov/oppsrrd1/registration\\_review/](http://www.epa.gov/oppsrrd1/registration_review/)). All pesticides distributed or sold in the United States generally must be registered by EPA. The decision to register a pesticide is based on the consideration of scientific data and other factors showing that it will not cause unreasonable risks to human health, workers, or the environment when used as directed on product labeling. The registration review program is intended to ensure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health and the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the new registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely.

As part of the implementation of the new Registration Review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the Agency is beginning its evaluation to determine whether tralomethrin continues to meet

the FIFRA standard for registration. This problem formulation for the environmental fate and ecological risk assessment chapter in support of the registration review is intended for the initial docket opening the public phase of the review process.

Deltamethrin, another registered active ingredient, is a major degradate of tralomethrin. In this assessment, only potential risk from deltamethrin as a degradate of tralomethrin will be addressed quantitatively, and the active ingredient deltamethrin will only be characterized qualitatively in the risk description. (For additional information about deltamethrin, please, refer to DP Barcode 373622.)

## **2.2. Mechanism of Action**

Tralomethrin and its major degradate, deltamethrin, are classified as a Type II synthetic pyrethroids, with a cyano group at the alpha-carbon position of the alcohol moiety. The primary biological effects of tralomethrin, and other pyrethroids, on insects and vertebrates reflect an inhibition of the correct firing of neurotransmitter deliver signals from one cell to another via nerve membrane inhibition of the voltage-gated  $\text{Ca}^{2+}$  channels (calcium ion channels) coupled with a stimulatory effect on the voltage-gated  $\text{Na}^{+}$  channels (sodium ion channels). The insecticidal effect of pyrethroids is characterized by a rapid "knock down," or paralysis, of insects. In insects, the type II pyrethroids predominantly cause ataxia and uncoordinated movement. All pyrethroids act as axonic poisons, affecting both the peripheral and central nervous systems, and share similar modes of action. Pyrethroids, including tralomethrin and deltamethrin, stimulate repetitive action in the nervous system by binding to voltage-gated  $\text{Na}^{+}$  channels, prolonging the  $\text{Na}^{+}$  ion permeability during the excitatory phase of the action potential. This action leads to spontaneous depolarizations, augmented neurotransmitter secretion rate and neuromuscular block, which ultimately result in paralysis of the insect.

## **2.3. Previous Risk Assessments**

Several reviews were available for tralomethrin (cotton – 03/05/84; soybeans – 12/03/85; cole crops, lettuce & sunflowers – 05/28/87 & 08/23/88; non-cropland – 03/02/92; logs & lumber – 11/17/93; review of new product containing tralomethrin, Scout-Xtra, 10/11/95). All reviews indicate that there is high concern for acute and chronic aquatic toxicity of tralomethrin. "The potential for substantial impact to aquatic fauna cannot be overstressed." Additional data were requested to negate the presumption of aquatic impacts and was made a condition for registration. Certain scenarios triggered acute and chronic levels of concern for aquatic invertebrates and chronic concerns for fish.

The latter risk assessments conducted on deltamethrin, a major degradate of tralomethrin, indicated risk concerns for organisms living in fresh and estuarine/ marine bodies of water. In addition, there were risk concerns for aquatic organisms living in the benthos.

### 1999 Scientific Advisory Panel on Sediment Toxicity and Fate of Synthetic Pyrethroids

A Scientific Advisory Panel (SAP) in 1999 examined the sediment toxicity and fate of synthetic pyrethroids. In response to a question regarding whether sediment toxicity data on one pyrethroid (cypermethrin) could be used to predict sediment toxicity to all pyrethroids, the panel generally supported the method of using data from a few pyrethroids to extrapolate information on toxicity to other pyrethroids. The panel recommended testing cypermethrin, "bifenthrin (relatively non-toxic to freshwater aquatic organisms, very insoluble in water, large bioconcentration factor) and possibly trefluthrin (highly toxic to freshwater aquatic organisms, stable in water, intermediate solubility in water to cypermethrin and bifenthrin)" (USEPA, 1999). The SAP also stated that a sediment:water ratio of 1 to 25 was acceptable for sediment toxicity tests.

The SAP commented on the use of  $K_d$  or  $K_{OC}$  to estimate concentrations of synthetic pyrethroids in sediments, recommending that the Agency reconsider  $K_{OC}$  as a measure of the binding potential of synthetic pyrethroids to sediment and soil because the use of  $K_d$  alone limits extrapolation to experimental conditions while  $K_{OC}$  "allows one to estimate partitioning across a wide variety of soil/sediment types" (USEPA, 1999). The Panel expressed concern that standard methods used to measure sorption may not be applicable to highly hydrophobic compounds due to high solids to water ratio, consideration of the character of the organic matter, presence of dissolved organic carbon, use of non-representative soils and sediments as sorbents, and improper methods used to measure organic carbon.

While the biota-sediment-accumulation-factor is a widely accepted method of assessment of bioaccumulation in sediments, the Panel indicated that the bioconcentration data for *Daphnia* and *Hyalella* should be sufficient to predict bioconcentration of pyrethroids. Finally, the Panel indicated that use of a solid phase microextraction (SMPE) method to determine the dissolved concentration in water could be used to account for sorption of pyrethroids to organic carbon and colloids present in the water column in the measurement of bioconcentration factors.

In 2003 and in response to the comments from the SAP on pyrethroids, EFED requested the following studies on esfenvalerate, cypermethrin, bifenthrin and cyfluthrin (Rexrode and Melendez, 2003).

#### **850.1735: Acute Sediment (freshwater)**

- Test organism: *Hyalella azteca* and *Chironomus tentans*
- Duration: 10 days, endpoint is survival.

#### **EPA/600/R01/020: Chronic Estuarine/Marine Sediment Testing**

- 28 day test on *Leptocheirus plumulosus*,
  - Percentage of neonates that survive as adults.
  - Growth rate.
  - Reproduction (#eggs/female, etc.).
  - Behavior.

A chronic 65-day freshwater test was also requested for cypermethrin only.

**EPA/600/R-991064: Chronic Freshwater Sediment Testing**

- 65 day test on *Chironomus tentans*
- Survival.
- Growth rate.
- Reproduction (# eggs/female, time to oviposition, proportion of females ovipositing, % hatch).

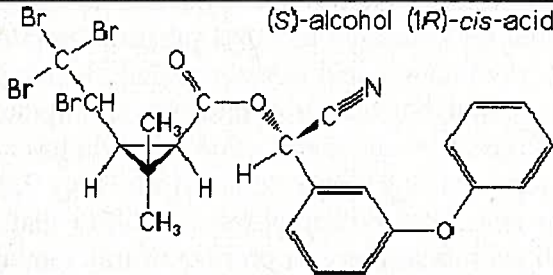
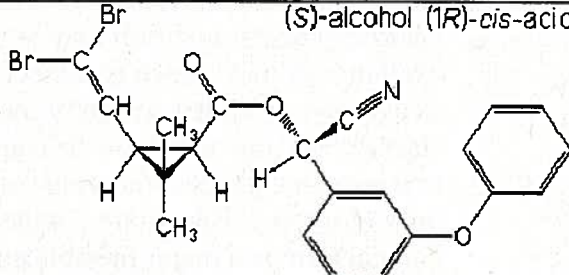
### **3. Stressor Source and Distribution**

Tralomethrin is a synthetic pyrethroid insecticide. Its structure has three rings, two phenyl rings attached to each other by an oxygen atom, and a cyclopropyl ring. It is cyano-substituted in the alpha position. The molecule has some chiral centers that result in stereoisomers. Chemically, it is the [1R, *cis*; alpha S]-isomer from 8 stereoisomeric esters of the 1,2,2,2-tetrabromoethyl-substituted analogue of chrysanthemic acid. The chemistry of tralomethrin may be dictated by its tetrabromoethyl substitution in the cyclopropyl ring, which is subject to debromination, and its ester moiety, which is subject to hydrolysis. Deltamethrin is another registered synthetic pyrethroid insecticide, with a similar structure to tralomethrin and similar stereochemistry. Tralomethrin has a 1,2,2,2-tetrabromoethyl substitution in the cyclopropyl ring, while deltamethrin has a 2,2-dibromoethenyl substitution at the same site. Environmental fate data show that deltamethrin is a major metabolism and photolysis reaction product of tralomethrin and it is also considered a stressor. There are many uncertainties related to the rate and extent at which tralomethrin undergoes debromination to form deltamethrin; however, despite these uncertainties, fate data suggest that this reaction occurs in a period of days to possibly several days or more, depending likely on factors such as media (soil, water or sediment), soil type (texture), pH, relative humidity and microbial biomass. The transformation of tralomethrin to deltamethrin does not appear to be immediate in the environment.

A summary of physicochemical properties of tralomethrin, and its major transformation product, deltamethrin, is included in **Table 3.1**.

For tralomethrin, the log  $K_{OA}$  is 15.4 (EPISuite v.4.0 estimate) and the log  $K_{OW}$  is 5.05. For chemicals that are not readily metabolized *in vivo*, a log  $K_{OA}$  and log  $K_{OW}$  in this range ( $K_{OA} > 5$ , log  $K_{OW} > 2$ ) have been associated with biomagnification in terrestrial-based food webs based on information presented in articles by Gobas *et al.* and Armitage & Gobas (2003 and 2007, respectively). However, pyrethroids, such as tralomethrin and the degradate deltamethrin, undergo substantial biotransformation *in vivo*. Even though the EFED has not adopted an official reference to distinguish chemicals that biomagnify, their presumption was utilized here as a general or broad reference to detect the biomagnification potential in terrestrial food chains.

**Table 3.1. Summary of physicochemical properties of tralomethrin and its degradate, deltamethrin.**

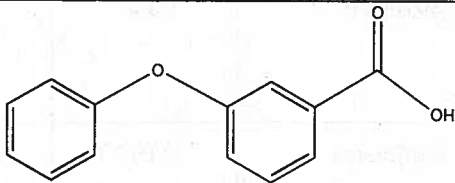
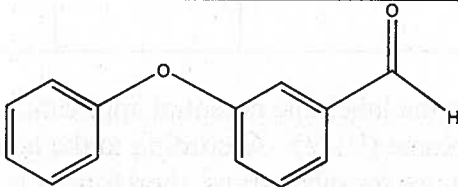
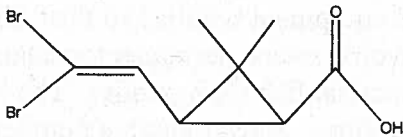
CHEMICAL	Parent - TRALOMETHRIN		Major Degradate - DELTAMETHRIN	
PARAMETER	VALUE(S) (units)	SOURCE	VALUE(S) (units)	SOURCE
CAS Chemical Name	(S)-cyano(3-phenoxyphenyl)methyl (1R,3S)-2,2-dimethyl-3-(1,2,2,2-tetrabromoethyl)cyclopropanecarboxylate	Tralomethrin data sheet (web): <a href="http://www.alanwood.net/pesticides/tralomethrin.html">http://www.alanwood.net/pesticides/tralomethrin.html</a> 06/23/09	(S)-cyano(3-phenoxyphenyl)methyl (1R,3R)-3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate	Deltamethrin data sheet (web): <a href="http://www.alanwood.net/pesticides/deltamethrin.html">http://www.alanwood.net/pesticides/deltamethrin.html</a> 06/23/09
IUPAC Chemical Name	(S)- $\alpha$ -cyano-3-phenoxybenzyl (1R,3S)-2,2-dimethyl-3-[(RS)-1,2,2,2-tetrabromoethyl]cyclopropanecarboxylate or (S)- $\alpha$ -cyano-3-phenoxybenzyl (1R)-cis-2,2-dimethyl-3-[(RS)-1,2,2,2-tetrabromoethyl]cyclopropanecarboxylate		(S)- $\alpha$ -cyano-3-phenoxybenzyl (1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate or (S)- $\alpha$ -cyano-3-phenoxybenzyl (1R)-cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate	
PC Code	121501	OPP Databases	097805	OPP Databases
Chemical Structure (from chemical's data sheet)	 <p>(S)-alcohol (1R)-cis-acid</p>		 <p>(S)-alcohol (1R)-cis-acid</p>	
CAS Reg. No.	66841-25-6	Laskowski, 2002	52820-00-5	Laskowski, 2002
Molecular Weight	665.0	Laskowski, 2002	505.2	Laskowski, 2002
Solubility	0.0840 mg/L or $8.40 \times 10^{-2}$ ppm at 25°C	Laskowski, 2002	0.000200 mg/L or $2.00 \times 10^{-4}$ ppm at 20°C	Laskowski, 2002
Vapor Pressure (25°C)	$1.8 \times 10^{-11}$ mmHg	Laskowski, 2002	$9.32 \times 10^{-11}$ mmHg	Laskowski, 2002
Henry's Law constant	$1.9 \times 10^{-10}$ Atm-m <sup>3</sup> /mol (Estimated from vapor pressure and water solubility)	Laskowski, 2002	$3.1 \times 10^{-7}$ Atm-m <sup>3</sup> /mol (Estimated from vapor pressure and water solubility)	Laskowski, 2002
Octanol-Water Partition Coefficient (log K <sub>ow</sub> and K <sub>ow</sub> at 20°C)	5.05 and $1.19 \times 10^5$	Laskowski, 2002	4.53 and $3.42 \times 10^4$	Laskowski, 2002

**Table 3.1. Summary of physicochemical properties of tralomethrin and its degradate, deltamethrin.**

CHEMICAL	Parent - TRALOMETHRIN		Major Degradate - DELTAMETHRIN	
PARAMETER	VALUE(S) (units)	SOURCE	VALUE(S) (units)	SOURCE
<b>Biomagnification Potential</b>	Presumption*: If $\log K_{OA} > 5$ , $\log K_{OW} > 2$ and the rate of chemical transformation is low, the chemical may biomagnify in terrestrial food chains.*	*Gobas <i>et al.</i> 2003 and Armitage & Gobas, 2007 support this presumption utilized here only as a broad reference to determine the potential for biomagnification.	Presumption*: If $\log K_{OA} > 5$ , $\log K_{OW} > 2$ and the rate of chemical transformation is low, the chemical may biomagnify in terrestrial food chains.*	*Gobas <i>et al.</i> 2003 and Armitage & Gobas, 2007 support this presumption utilized here only as a broad reference to determine the potential for biomagnification.
	For tralomethrin, $\log K_{OA}=15.4$ , $\log K_{OW}=5.05$ & rate of transformation is moderate in the environment; it appears that tralomethrin has a potential to biomagnify in terrestrial food chains.		For deltamethrin, $\log K_{OA}=9.89$ , $\log K_{OW}=4.53$ & rate of transformation is relatively low in the environment and appears to be moderate in fish; it appears that deltamethrin has a potential to biomagnify in terrestrial food chains.	

Even though some other degradates were observed in the laboratory studies (e.g. 3-PBA and tetramethrinic acid or Br<sub>2</sub>CA), it was found that they were the result of the rupture of the ester bond of the parent molecule. It is believed that the resulting molecules are not as toxic as the parent because they presumably have lost their mode of action. **Table 3.2** shows the chemical structures of the other major degradation products of tralomethrin & deltamethrin. At this time, they are not considered stressors.

**Table 3.2. Major transformation products of tralomethrin**

Common Name	Chemical Name	Structure
m-PBA or 3-PBA or 3-PBAcid (CAS No. 3739-38-6)	3-phenoxybenzoic acid	
3-PBAlddehyde (CAS No. 39515-51-0)	3-phenoxybenzaldehyde	
Decamethrinic Acid or Br <sub>2</sub> CA (CAS No. 53179-78-5)	Product of aerobic soil metabolism, DBVA = 3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane-carboxylic acid; Product of hydrolysis = (1R-cis)-3-(2,2-dibromoethyl)-2,2-dimethylcyclopropanecarboxylic acid (one form of Br <sub>2</sub> CA)	

In addition, various isomers of deltamethrin have been observed in studies conducted with the major transformation product. One such example is *alpha*-R-deltamethrin.

### 3.1. Overview of Pesticide Usage

A summary table of all agricultural use patterns for tralomethrin follows (Table 3.3).

<b>Table 3.3. Summary of agricultural use information for tralomethrin, based on Scout X-TRA® Insecticide label (EPA Reg. No. 34147-3) and LUIS Report.</b>						
USE	SINGLE APP. RATE (lb. a.i./A)	NUMBER OF APPS.	SEASONAL APP. RATE (lb. a.i./A)	INTERVAL BETWEEN APPS. (days)	APP. METHOD	PRE HARVEST INTERVAL (days)
Broccoli	0.024	8	0.19	As Needed	Aerial or Ground Spray & ULV	5
Cotton	0.024	8	0.19	5	Aerial or Ground Spray & ULV	28
Lettuce	0.024	8	0.19	As Needed	Aerial or Ground Spray & ULV	3
Soybeans	0.024	5	0.12	As Needed	Aerial or Ground Spray & ULV	21
Sunflowers	0.019	3-4	0.060	As Needed	Aerial or Ground Spray	21

For the label, the potential application methods are ground and aerial spray, or Ultra-Low Volume (ULV). According to the label, ULV applications are precluded for sunflowers, but not for other crops, therefore, it is presumed that they are allowed for crops other than sunflowers. The labels for tralomethrin require a buffer zone, according to the method of application. The product should not be applied by ground equipment within 25 ft or by aerial equipment within 150 ft of freshwater or estuarine/ marine bodies of water (lakes, reservoirs, rivers, permanent streams, marshes or natural ponds, and estuaries or commercial fish farm ponds). The buffer zone should be increased to 450 ft for ULV applications. Even though a number of synthetic pyrethroids have the requirement of a 10 ft zone around permanent bodies of water so as to allow growth of a maintained vegetative filter strip, the label for tralomethrin does not have this specific requirement. One important restriction of the label, for the use on cotton, is that not more than 10 applications of synthetic pyrethroids are allowed in a growing season.

Inspection of the use information for tralomethrin and deltamethrin found one product that contains both active ingredients. Deltamethrin is the major degradate of tralomethrin in the environment. The product, HR 20900 (EPA Reg. No. 34147-10), is for use on cotton via ground or aerial applications (no ULV). The product contains 1 lb a.i./gallon (0.5 lb of tralomethrin and 0.5 lb of deltamethrin/gallon) and the maximum seasonal total application rate is 0.20 lb a.i./A/growing season.

Available toxicity data for environmental mixtures of tralomethrin with other pesticides will be presented as part of the ecological risk assessment. It is expected that the toxic effect of tralomethrin, in combination with other pesticides used in the environment, is likely to be a function of many factors including but not necessarily limited to: (1) the exposed species, (2) the co-contaminants in the mixture, (3) the ratio of tralomethrin and co-contaminant concentrations, (4) differences in the pattern and duration of exposure among contaminants, and (5) the differential effects of other physical/chemical characteristics of the receiving waters (*e.g.* organic matter present in sediment and suspended water). Quantitatively predicting the combined effects of all these variables on mixture toxicity to any given taxa with confidence is beyond the capabilities of the available data and methodologies. However, a qualitative discussion of implications of the available pesticide mixture effects data regarding the confidence of risk assessment conclusions will be addressed as part of the uncertainty analysis.

Piperonyl butoxide and MGK are commonly used in formulations with pyrethroids. Piperonyl butoxide acts as a potentiator in both mammals and insects because the pyrethroid is not metabolized and excreted as quickly (Barile, 2004; Hodgson and Smart, 2001). Exposure to pyrethroids along with piperonyl butoxide increases the toxicity of the pyrethroids (Weston & Lydy, 2010). MGK-264, another potentiator/synergist used with pyrethroids, has similar effects as those observed for piperonyl butoxide (Hodgson and Smart, 2001). No current tralomethrin registrations exist for a product with piperonyl butoxide. One active product registration exists for formulation of MGK and tralomethrin (Reg. # 9688-151).

The Agency routinely assesses potential exposure to formulations by examining acute exposure to spray drift. Acute toxicity data on the formulation is compared to potential exposure to spray drift. The sole active tralomethrin registration that contains MGK is a residential spray can use. The spray drift associated with this use will be minimal. Therefore, a quantitative assessment of the potential aquatic exposure to the formulation containing MGK is not necessary. However, piperonyl butoxide and/or MGK from other pyrethroid applications could interact with tralomethrin in the environment or the additives could be applied co-currently as a tank mix. Therefore, potential interactions will be discussed qualitatively in the risk assessment.

The Screening Level Usage Analysis (SLUA) summary for tralomethrin is as follows (Table 3.4):

**Table 3.4. Screening-Level Estimates of Agricultural Uses for Tralomethrin (SLUA, dated 04/07/09)**

Crop	lb a.i.	Percent (%) Crop Treated	
		Average	Maximum
Broccoli	<500	5	10
Cauliflower+	<500	<2.5	<2.5
Cotton	3,000	<1	<2.5
Lettuce	<500	<2.5	<2.5
Peanuts+	<500	<1	<2.5
Sunflowers	<500	<1	<2.5

The sources of the SLUA include the United States Department of Agriculture's National Agricultural Statistics Service (USDA-NASS), the National Pesticide Use Database (NPUD) of the CropLife America Foundation and California Department of Pesticide Regulation (CDPR) data. The information is amalgamated and put in a public releasable format.

+ These crops were not known to be listed on active end use product registrations when this report was run. All numbers rounded.

'<500' indicates less than 500 pounds of active ingredient. '<2.5' indicates less than 2.5 percent of crop is treated. '<1' indicates less than 1 percent of crop is treated.

The U.S. Geological Survey (USGS) pesticide use maps show regional scale patterns in use intensity within the United States. The USGS pesticide maps are based on State level estimates of pesticide use rates for individual crops, which have been compiled by the National Center for Food and Agricultural Policy (NCFAP) for 1999 through 2004, and on the 2002 Census of Agriculture for county crop acreage crop.

For tralomethrin (**Fig. 3.1**), four uses were found to be important: cotton, soybeans, lettuce and broccoli. Of these, the former two cover almost all the use (around 61% and 37%, respectively), of the total of 5964 lb applied. A large use region of the US is covered by the map, including the region of the Mississippi river and delta – AR, MS and LA – and a belt covering the states of AL GA, NC, SC and the north of FL. Tralomethrin was also used in a small region of coastal CA.

## TRALOMETHRIN - insecticide

2002 estimated annual agricultural use

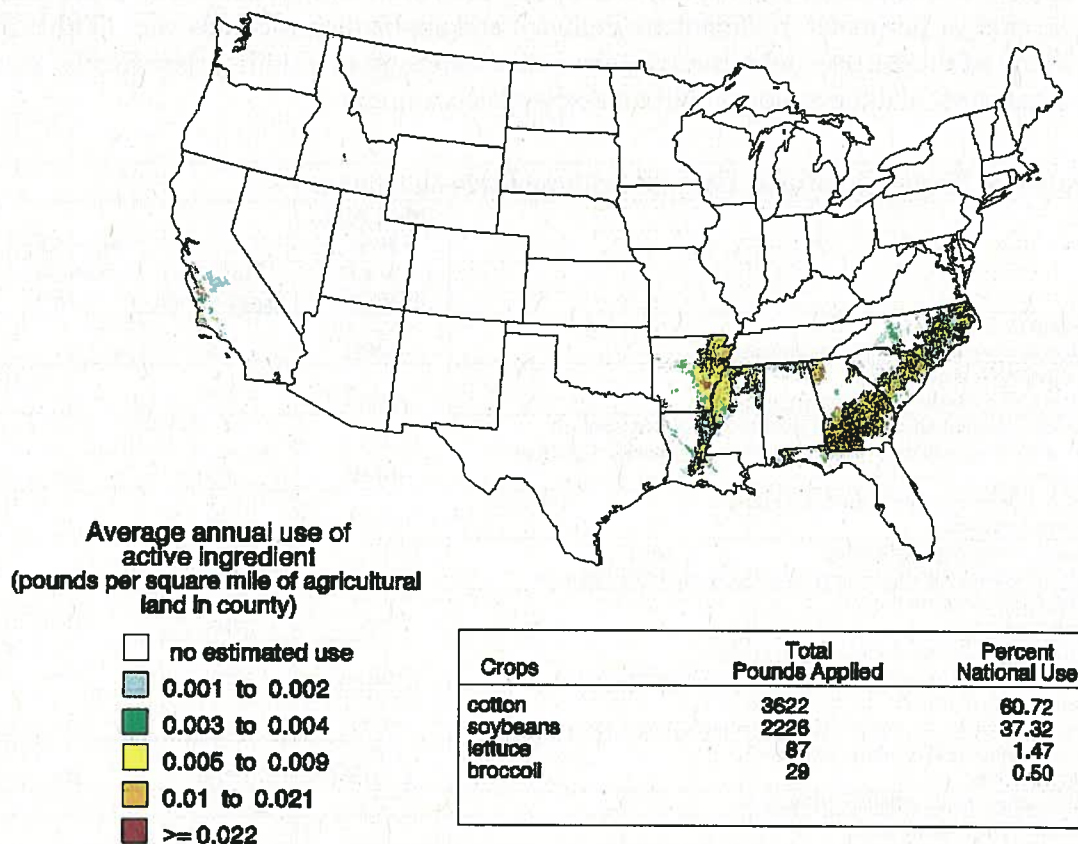


Fig. 3.1. Use of Tralomethrin in 2002

Note of Caution: The pesticide use maps available from the web ([http://water.usgs.gov/nawqa/pnsp/usage/maps/compound\\_listing.php?year=02](http://water.usgs.gov/nawqa/pnsp/usage/maps/compound_listing.php?year=02)) show the average annual pesticide use intensity expressed as average weight (in pounds) of a pesticide applied to each square mile of agricultural land in a county. The area of each map is based on state-level estimates of pesticide use rates for individual crops that were compiled by the CropLife Foundation, Crop Protection Research Institute during based on information collected during 1999 through 2004 and on 2002 Census of Agriculture county crop acreage. The maps do not represent a specific year, but rather show typical use patterns over the five year period 1999 through 2004. Use intensity rates are expressed as the pounds applied per square mile of mapped agricultural land in a county. The area of mapped agricultural land for each county was obtained from an enhanced version of the 1992 USGS National Land Cover Data (NLCD). The key limitations of the data used to produce these maps include the following: (1) state use coefficients represent an average for the entire state and consequently do not reflect the local variability of pesticide management practices found within states and counties, (2) pesticide use estimates are not for a specific year, but represent typical use patterns for the five year period, (3) state pesticide use coefficients may not have been available for all states where a pesticide may have been applied to agricultural land, and therefore, are not displayed on the maps, (4) the county crop acreage is based on the 2002 Census of Agriculture and may not represent all crop acreage because of Census nondisclosure rules, and (5) agricultural land area used to calculate the pesticide use intensity and display the data was derived from 30-meter satellite remote sensing data that may over estimate or underestimate the actual agricultural land area. The maps are not intended for making local-scale estimates of pesticide use, such as estimates at the county level. Please refer to [Method for Estimating Pesticide Use](#) for a detailed discussion of how the pesticide use data were developed.

In addition to the classical agricultural use sites, tralomethrin has multiple urban uses. Many of these uses are classified as outdoor residential such as household/ domestic dwellings, ornamental and/ or shade trees, ornamental ground cover, ornamental herbaceous plants, lawns and turf, pet living/ sleeping quarters, garbage cans, paths/ patios, and wood protection treatment. Other uses are terrestrial non-food, such as

industrial areas outdoor, non-agricultural outdoor buildings/ structures, ornamental lawn, turf, non-flowering plants, woody shrubs and vines, paved areas (roads/ sidewalks) and solid waste sites. According to the LUIS report, in many instances, the maximum application rate is 0.0051 lb a.i./1000 sq. ft. Uses such as spot treatment, crack and crevice, or perimeter treatment are included and application methods vary (**Table 3.5**). Many of these uses could involve substantive exposure to wildlife, specifically, aquatic organisms, and the majority will be assessed accordingly.

**Table 3.5. Nonagricultural Uses of Tralomethrin Outdoors**

Use	Max. App. Rate (lb a.i./ 1000 ft <sup>2</sup> )*	Max. No. Apps./ Year	Max. App. Rate per Year	Min. App. Int./ days
Agricultural/ farm premise				
Outdoor premise treatment/ Perimeter treatment	0.0051	NS	NS	NS
Barns/barnyards/auction barns				
Outdoor premise treatment/ Perimeter treatment	0.0051	NS	NS	NS
Commercial/institutional/industrial premises/equipment (outdoor)				
Crack and crevice and/or spot treatment/ Perimeter treatment/ premise treatment	0.0041	NS	NS	NS
Food stores/markets/supermarkets premises				
Perimeter treatment	NS	NS	NS	NS
Horses (show/race/special/ponies)				
Crack and crevice and/or spot treatment/ Outdoor premise treatment	0.0051	NS	NS	NS
Household/domestic dwellings				
Perimeter treatment	NS	NS	NS	NS, 14 & 28
Household/domestic dwellings outdoor premises				
Broadcast, mound drench, spot treatment, outdoor general surface	Various	NS	NS	NS and AN
Industrial areas (outdoor)				
Outdoor general surface spray/ Outdoor treatment/ Perimeter treatment	0.0050	NS	NS	NS
Nonagricultural areas (public health use)				
Mound treatment	0.0041 lb/mound	NS	NS	NS
Nonagricultural outdoor buildings/structures	NS	NS	NS	NS
Ornamental and/or shade trees				
Outdoor treatment/ Perimeter treatment/ mound drench	Various	NS	NS	NS
Ornamental ground cover	NS	NS	NS	NS
Ornamental herbaceous plants				
Perimeter treatment, Outdoor treatment	0.0024 and various	NS	NS	NS
Ornamental lawns and turf				
Mound drench	0.0100 and 0.0041 lb/mound	NS	NS	NS
Ornamental nonflowering plants				
	0.0021 and various	NS	NS	NS
Ornamental woody shrubs and vines				
Outdoor treatment/ Perimeter treatment/ Mound drench	0.0051 & 0.0041 lb/mound	NS	NS	NS
Paths/ Patios				
Outdoor premise treatment/ Perimeter treatment/ Mound drench	0.0051 & 0.0041 lb/mound	NS	NS	NS
Paved areas (private roads/sidewalks)				
Outdoor general surface spray/ Outdoor premise treatment/ Perimeter treatment/ Mound drench	0.0051 & 0.0041 lb/mound	NS	NS	NS
Pet living/sleeping quarters				
Outdoor general surface spray/ Spot treatment	NS	NS	NS	14, 28, AN, NS
Public buildings/structures (vert. pest control)				
Outdoor general surface spray/ Perimeter treatment	0.0050	NS	NS	NS
Refuse/solid waste sites (outdoor)	0.0051	NS	NS	NS
Residential lawns	Various	NS	NS	NS
Sewage systems				
Perimeter treatment	0.0051	NS	NS	NS
wood protection treatment to buildings/products outdoor				
Soil treatment/ Injection treatment	Various	NS	NS	NS

NS = Not Specified; AN = As Needed;

**Table 3.5. Nonagricultural Uses of Tralomethrin Outdoors**

Use	Max. App. Rate (lb a.i./ 1000 ft <sup>2</sup> )*	Max. No. Apps./ Year	Max. App. Rate per Year	Min. App. Int./ days
* 0.0051 lb/1000 ft <sup>2</sup> is equivalent to 0.22 lb a.i./A; Data obtained from LUIS Report.				

In addition, there are numerous indoor non-food use sites like for example, agricultural farm premises (indoor), autos, recreational vehicles, ships, boats, caskets, warehouse premises and equipment (indoors and outdoors), eating establishments, egg packing plants, food processing plants and premises, food stores, grain products (processed), greenhouses, hospital/ medical institutions, household/ domestic dwellings, meat processing plants, poultry processing plant premises and public buildings/ structures. These labeled uses will be assessed only qualitatively in the ecological risk assessment, as they present minimal chance for exposure to nontarget organisms in aquatic or terrestrial environments.

In a recent study (Stout II, *et al.* 2009), conducted by the US Department of Housing and Urban Development, in collaboration with the USEPA, several chemicals were surveyed on floors of occupied homes. The survey included several synthetic pyrethroids like deltamethrin, which is the major transformation product of tralomethrin. Deltamethrin was detected with a frequency of 27%, illustrating the prevalence of these chemicals. Weston *et al.* 2005, studied the presence of synthetic pyrethroids in Roseville, CA, selected as a typical suburban development. Sediments from creeks that drain subdivisions of single-family homes were found to be toxic to *Hyaella azteca*. The synthetic pyrethroids were considered to be the primary cause of the toxicity. Amweg *et al.* 2006, also studied synthetic pyrethroids in urban areas of CA and TN. Deltamethrin was found to be a contributor to the toxicity of sediments sampled. These are just a few examples that illustrate the high use of synthetic pyrethroids in urban settings and potential toxicity to nontarget organisms.

### 3.2. Environmental Fate and Transport

A summary of environmental fate/ transport properties of tralomethrin, and its major transformation product, deltamethrin, and two other major degradates, Br<sub>2</sub>CA and 3-PBA, is included in **Table 3.6**.

**Table 3.6. Summary of Environmental Fate and Transport Properties of Tralomethrin, its Major Transformation Product, Deltamethrin, and Two Other Major Degradates BR<sub>2</sub>CA and 3-PBA.**

Chemical	TRALOMETHRIN		Transformation Product – DELTAMETHRIN	
PARAMETER	VALUE(S) (units)	SOURCE	VALUE(S) (units)	SOURCE
<b>Hydrolysis Half-life pH 5, 7, 9; (25°C)</b>	Data suggest that tralomethrin half-lives are >30 d; while for other study, data suggest that tralomethrin is ~ stable at pH 4 and 5, and undergoes some reaction at pHs 7 and 9.  *Deltamethrin (and related compounds), $\alpha$ -R-deltamethrin and BR <sub>2</sub> CA.	MRIDs 58862 & 58907; MRID 44814501 – U  <u>A new study is required.</u>	Stable at pH 5 and 7. Half-life of 2.5 days at pH 9.  BR <sub>2</sub> CA and m-PBAlddehyde	MRID 41651038
<b>Aqueous Photolysis Half-life (pH 5)</b>	Possibly moderate to very fast reaction.  *R-tralomethrin, deltamethrin-iso (deltamethrin and related moieties) and BR <sub>2</sub> CA	J. Agric. Food Chem. 29(4) 1981, Acc. No. 258017, MRID 44814502 – U  <u>A new study is required.</u>	64 and 84 days for benzyl and gem labels, respectively; relatively stable.  *cis-BR <sub>2</sub> CA	MRID 42114818
<b>Soil Photolysis Half-life</b>	Uncertain rate of reaction.  *R-tralomethrin, deltamethrin-iso (deltamethrin and related moieties)	MRID 146120, MRID 44814503 – U  <u>A new study is required.</u>	The half life was 9 days, but, at the end of the 30 day study, both the irradiated and dark control samples had around the same amount of parent material. Considered stable to photodegradation on soil.	MRID 42114819
<b>Aerobic Soil Metabolism Half-life</b>	16-32 d in SiL and <32 d, <64 d and <128 d in SiL, SL and SiL, respectively, based on <sup>12</sup> CO <sub>2</sub> evolution.  In a SL, based on 0-7 d data, 3.1-3.2 days – Laskowski, 2002 reports 24.2 days.  *Deltamethrin (max. 52.4%, it degraded w. half-lives of 31.3 and 34.9 d) and cis-BR <sub>2</sub> CA (27.6%) were the major products.	MRIDs 58859, 132549 – S, MRID 44814504  <u>A study conducted with three soil systems is required.</u>	Dubbs fine SL and Memphis SiL, half-lives 11-19 days; alkaline Arizona SL half-lives 22 and 26 days	MRID 41677404, 41677407
<b>Anaerobic Soil Metabolism Half-life</b>	35 to 69 d for SiL & SL soil systems, respectively; tetrabromocyclopropane-carboxylic acid (decreased over time) and cis- and trans-dibromocyclopropane-carboxylic acid were observed. It appears that the method does not distinguish between tralomethrin and deltamethrin.  SL system – the parent was observed only at 0-3 days. When anaerobic conditions were induced, no tralomethrin was detected at 30 days. Half-lives for tralomethrin plus deltamethrin were 33.5 and 35.6 d.  *deltamethrin was major and half-lives were 42.9-46.7 days; also 3-PBA (20.6%) and BR <sub>2</sub> CA (40.6-57.0%)	Acc. No. 255882, MRID 132767 & 152021  MRID 44814505 – S	Alkaline SL half-lives 32-36 days.  (In the study conducted w. tralomethrin, deltamethrin was major degradate, with half-lives of 42.9-46.7 days – see additional details on the left column)..	MRID 42114821, 44814505; Acc. No. 255882, MRID 132767 & 152021

**Table 3.6. Summary of Environmental Fate and Transport Properties of Tralomethrin, its Major Transformation Product, Deltamethrin, and Two Other Major Degradates Br<sub>2</sub>CA and 3-PBA.**

Chemical	TRALOMETHRIN		Transformation Product – DELTAMETHRIN	
PARAMETER	VALUE(S) (units)	SOURCE	VALUE(S) (units)	SOURCE
Anaerobic Aquatic Metabolism Half-life	Tralomethrin + Deltamethrin 6 systems ave=85.9 d	Kaufman, et al., Unk. Yr. – a study referenced by Laskowski 2002 <u>A study is required.</u>	NA	NA
Aerobic Aquatic Metabolism Half-life	NA	<u>A study is required.</u>	System I, L: 25.9 days System II, SL: 120 days *Major – $\alpha$ -R-deltamethrin (21-24% at 7-14 d). Systems from the Netherlands	MRID 44977005
Organic Carbon Partition Coefficient for Parent ( $K_{oc}$ )	333000, 87700, 43800, 676000 mL/g <sub>oc</sub> for S, SL, L and CL (in sterile soils)	MRID 44814506 – S	392000, 577000, 204000, 460000 mL/g <sub>oc</sub> Two SiL soils, a SL, and a SiCl	MRID 41651039, 42475908, 42976501
Soil Partition Coefficient for Parent ( $K_p$ )	832, 3510, 197, 8780 mL/g for S, SL, L and CL (in sterile soils)	MRID 44814506 – S	3000, 4750, 960, 3790 (SiCl) mL/g Two SiL soils, a SL, and a SiCl	MRID 41651039, 42475908, 42976501
Terrestrial Field Dissipation Half-life	Corn and bareground plots with loam soils in CA – half-life for combined residues of tralomethrin and deltamethrin is 19.8 days.  LS in CA – bareground and cotton, respective half-lives of 2.4 and 1.5 days. Total residues (cis-deltamethrin + tralomethrin) dissipated with respective half-lives of 12.4 and 13.9 days, for bareground and cotton plots.	MRID 44814507 – S; 44814508	Louisiana cotton 231 days, long half-life observed, both for the bareground and the cropped plot.  California cotton 37 d for bareground plot, and 40 d for cropped plot.  Minnesota corn 69 d for bareground plot, and 14 days for the cropped plot.	MRID 42137505, 42773903, 42114822
Bioaccumulation in Fish (BCF)	490X, 68X, 920X for whole fish, edible and non-edible tissues, respectively. Residues were equal amounts of tralomethrin, and a pyrethroid-like cpd. such as 1'-bromo-deltamethrin. After 21 d, 89% of residues were eliminated. Calculated depuration half-life is 6.4 d.	Acc. No. 072124, 288552 or MRID 152024	698X whole body, 189X edible portion, depuration was moderately slow (50% between 3-7 days, and 70-75% after 2 weeks)	MRID 43072701, 43072702, 41651040
Parameter\ Chemical	m-phenoxybenzoic Acid (m-PBA or 3-PBA)		Br <sub>2</sub> CA (decamethrinic acid, RU 23441)	
Organic Carbon Partition Coefficient ( $K_{oc}$ )	288, 190, 105, 50.7 mL/g <sub>oc</sub> (for Cl, SiCIL, SL & CIL)	MRID 44977006	38.2, 46.8, 43.7, 23.0, 10.1 mL/g <sub>oc</sub>	MRID 42475908
Soil Partition Coefficient ( $K_d$ )	0.668, 1.54, 2.68, 1.34 mL/g (for Cl, SiCIL, SL & CIL)	MRID 44977006	0.09, 0.11, 0.36, 0.59, 0.27 mL/g	MRID 42475908
Notes	<u>For tralomethrin</u> , various studies that were deemed supplemental or unacceptable were identified with S or U, respectively.			

When applied to the field, tralomethrin, and its major degradate, deltamethrin, are likely to partition to the soil and organic matter in the crops; tralomethrin and deltamethrin appear to bind strongly to soil and organic matter, though binding may not be instantaneous ( $K_{oc} \gg 40,000$ , hardly mobile to immobile). It is not expected to leach into subsurfaces. It

may reach aquatic environments via spray drift or in runoff events accompanied by erosion. The persistence of tralomethrin is uncertain. In an aerobic soil metabolism study, its half-lives were 3.1-3.2 days. Deltamethrin, the major transformation product, appears to be moderately to highly persistent in terrestrial environments (aerobic soil metabolism 11-26 days; terrestrial field dissipation 14-231 days). It has the potential to persist in aquatic environments, where it may partition with the sediment and has the potential to affect benthic and epibenthic organisms (aerobic aquatic metabolism 26-120 days; anaerobic soil metabolism 32-36 days). Due to their low Henry's Law Constants, tralomethrin and deltamethrin are unlikely to volatilize substantially ( $1.9 \times 10^{-10}$  and  $3.1 \times 10^{-7}$  atm-m<sup>3</sup>/mol, respectively).

There are many uncertainties related to the rate and extent at which tralomethrin undergoes transformation to deltamethrin. For various of the fate studies, the methods could not distinguish these chemicals from each other, and an overall rate of transformation is available. An aerobic soil metabolism study yielded a half-life of 3.1-3.2 days in a sandy loam (based on 0-7 day data), and results of terrestrial field dissipation studies indicated half-lives of 1.5-2.4 days (cotton plot and bareground of loamy sand in California). Both studies appear to be consistent with each other. In general, it appears that the rate of transformation of tralomethrin to deltamethrin is in the range of days to possibly several days, and not an immediate reaction, depending on factors such as media (soil, water or sediment), soil type, pH, relative humidity of the soil, microbial biomass, and other factors.

Previously reported data suggest that tralomethrin is stable to hydrolysis at pHs 3-5, but may be more prone to reaction at pHs 7-9 (reaction rate is uncertain). Major hydrolysates may be deltamethrin (and related compounds, including  $\alpha$ -R-deltamethrin) and (1R-cis)-3(2,2-dibromo-ethyl)-2,2-dimethyl-cyclopropanecarboxylic acid (BR<sub>2</sub>CA). Subsequently, the degradate deltamethrin is relatively stable at pH 5 and 7. However, it rapidly degraded (half-life of 2.5 days) at an alkaline pH of 9 to form Br<sub>2</sub>CA, <0.15 ug/L and 3-phenoxy-benzaldehyde (3-PBaldehyde, 3.42 ug/L).

Available data suggest that upon aqueous and soil photolysis, tralomethrin may undergo epimerization (to R-tralomethrin) and subsequent transformation to deltamethrin-iso (deltamethrin and related moieties), and formation of BR<sub>2</sub>CA. The rates of reaction are uncertain: it appears to be relatively fast in water. Subsequently, deltamethrin does not appear to photodegrade substantially in aqueous solutions (half-lives 64 & 84 days). Although the soil photolysis study on deltamethrin yielded a half-life of 9 days, considerable degradation was occurring in the dark controls as well.

Based on acceptable aerobic soil metabolism data, in a sandy loam, half-lives were 3.1-3.2 days, based on 0-7 d data (note, Laskowski\* reports 24.2 days). Major degradates were deltamethrin (max. 52.4%, it degraded with half-lives of 31.3 and 34.9 days) and cis-BR<sub>2</sub>CA (27.6%). In a supplemental study, based on <sup>14</sup>CO<sub>2</sub> evolution, half-lives for residues were 16-32 days in silt loam, and <32 days, <64 days and <128 days in silt loam, sandy loam and silt loam, respectively. The major degradate, deltamethrin, in Dubbs fine sandy loam and Memphis silt loam soil degraded rapidly (half-life 11-19 days) to form

Br<sub>2</sub>CA (<10%) and CO<sub>2</sub>. Over the 128 day incubation period, 62-77% and 52-60% of the <sup>14</sup>C-cyano- and the <sup>14</sup>C-phenoxy-labelled parent evolved as <sup>14</sup>CO<sub>2</sub>. The proposed routes of degradation are ester hydrolysis and microbial-mediated mineralization to CO<sub>2</sub>. An additional aerobic soil metabolism study was submitted for deltamethrin in an alkaline Arizona sandy loam (pH 8.1), which yielded half-lives of 22 and 26 days. For the gem label study, Br<sub>2</sub>CA was formed, which peaked at 23-26% on day 30 and 14, respectively. It is noted that despite the fact that the pH of the latter study was higher, the half-lives were higher as well, which was contrary to what was expected from the hydrolysis study.

There is no aerobic aquatic metabolism study for the parent, tralomethrin. The degradate, deltamethrin, in an aerobic aquatic metabolism study, consisting of a loam or a sandy loam test systems from the Netherlands, degraded with respective half lives for the whole systems of 26 and 120 days. The major transformation product was the α-R-deltamethrin, at up to 24% in the SL. There is no anaerobic aquatic metabolism study available, but Laskowski, 2002 references a study that yielded a half-life for total tralomethrin plus deltamethrin of 85.9 days (average of six systems).

In a sandy loam system, the parent was observed only at 0-3 days of aerobic incubation. At 3 days, anaerobic conditions were induced but no tralomethrin was detected at 30 days post-flooding (which was the next test interval). Half-lives for tralomethrin plus deltamethrin were 33.5 and 35.6 days. Deltamethrin was the major product and half-lives for the deltamethrin were 42.9-46.7 days. Other major products were 3-phenoxybenzoic acid (3-PBA, 20.6%) and BR<sub>2</sub>CA (40.6-57.0%). In an anaerobic soil metabolism study conducted on the degradate deltamethrin, the chemical degraded in an AZ sandy loam (pH 8.1) with a half-life of 32-36 days for the benzyl and gem labels, respectively. For the gem label experiment, only one metabolite, Br<sub>2</sub>CA or decamethrinic acid, was found at 49% of the applied radioactivity by day 30 and remained at about this level on days 59 (52%) and 90 (48%). For the benzyl label, 3-PBA was a minor metabolite.

In batch equilibrium studies, tralomethrin residues were found to be hardly mobile to immobile (FAO classification), in sterile soils, with K<sub>FOC</sub>'s range of 43,800-676000 and had Freundlich K<sub>F</sub>'s of 832, 3510, 197 and 8780 for a sand, sandy loam, loam and clay loam soils, respectively. K<sub>F</sub>'s correlated with organic matter and clay content [respective coefficients of determination (or r<sup>2</sup>) of 0.85 and 0.92], but did not correlate with pH (coefficient of correlation of 0.029). In batch equilibrium studies, deltamethrin was found to be immobile (K<sub>FOC</sub>>100,000, FAO classification) and had Freundlich K<sub>F</sub>'s of 3,790 for a MS silty clay loam, 3000 for an AK silt loam, 4750 for a GA silt loam, and 960 for a TX sandy loam. K<sub>FOC</sub>'s ranged from 204000 to 577000. Although deltamethrin is tightly bound, adsorption is not immediate, because equilibrium times were 4-24 hours.

In corn and bareground plots with loam soils in CA – half-life for combined residues of tralomethrin and deltamethrin is 19.8 days. In a loamy sand in CA – for bareground and cotton, respective half-lives were 2.4 and 1.5 days. Total residues (cis-deltamethrin + tralomethrin) dissipated with respective half-lives of 12.4 and 13.9 days, for bareground and cotton plots. In three terrestrial field dissipation studies conducted on deltamethrin, it appeared not to be mobile in soil and degraded with half-lives of 37 and 40 days for

bareground and cotton plots, respectively, in CA. In MN, half-lives were 69 and 14 days for bareground and corn plots, respectively. In the Louisiana study, the half-life was almost 8 months, both for bareground and cotton plots. The longer half-life could fall within the range of normal field variability and the Louisiana soil was the lowest in organic matter, which would result in the lowest amount of soil binding and soil microbial degradation. No clear pattern of degradate formation and decline was seen, possibly because the low application rate and 6" sampling depths resulted in soil dilution, so degradates were not detected.

The tralomethrin maximum bioconcentration factors (BCFs) were 490X, 68X, 920X for whole fish, edible and non-edible tissues, respectively. Residues were equal amounts of tralomethrin and a pyrethroid-like compound, such as 1'-bromo-deltamethrin. After 21 days, 89% of residues were eliminated. Calculated depuration half-life is 6.4 days. In another fish bioconcentration study, the degradate deltamethrin had bioconcentration factors of 189x and 3630x in edible and visceral fish tissues, respectively. The whole body BCF of 698x was estimated from edible and visceral fish tissue results. The majority of the radioactive residue found in fish was deltamethrin, accounting for 78 and 83% of the total radioactive residue in edible and visceral fish tissues, respectively. Depuration was not studied; however, the depuration from a previous study submitted was considered (about 50% between days 3-7 and 70-75% after 2 weeks of depuration).

**Tables 3.7- 3.8** provide a summary of the various degradation products formed by each process in the studies reviewed for tralomethrin and deltamethrin, respectively.

Table 3.7. Summary of degradate formation from degradation of tralomethrin.				
STUDY TYPE	DEGRADATE and MAXIMUM CONCENTRATION			SOURCE
	Deltamethrin, Br <sub>2</sub> CA, 3–PBA (% applied)			
Hydrolysis	Deltamethrin (and related compounds), α-R-deltamethrin and Br <sub>2</sub> CA			MRID 44814501 – U
Aqueous Photolysis	R-tralomethrin, deltamethrin-iso (deltamethrin and related moieties) and Br <sub>2</sub> CA			MRID 44814502 – U
Soil Photolysis	R-tralomethrin, deltamethrin-iso (deltamethrin and related moieties)			MRID 146120 & 44814503 – U
Aerobic Soil Metabolism	Deltamethrin (max. 52.4%)	cis-Br <sub>2</sub> CA (27.6%)	–	MRIDs 58859, 132549– S & 44814504
Anaerobic Soil Metabolism	Deltamethrin (59.0%)	Br <sub>2</sub> CA (40.6-57.0%)	3-PBA (20.6%)	MRID 132767 & 152021, and 44814505 – S
Terrestrial Field Dissipation	Deltamethrin	–	–	MRID 44814507 – S, & 44814508

Table 3.8. Summary of degradate formation from degradation of deltamethrin.				
STUDY TYPE	DEGRADATE and MAXIMUM CONCENTRATION			SOURCE
	Br <sub>2</sub> CA, 3-PBA, 3-PBAldehyde, α-R-Deltamethrin (% applied)			
Hydrolysis	Br <sub>2</sub> CA <0.15 ug/L (app. rate 10.0 ug/L)	3-PBAldehyde 3.37 ug/L at 30 days (app. rate 10.0 ug/L)	—	MRID 41651038
Aqueous Photolysis	cis-Br <sub>2</sub> CA at day 21	3-PBA 11% at day 21	—	MRID 42114818
Soil Photolysis	trans-Br <sub>2</sub> CA 53.9% at 30 days	—	α-R-deltamethrin	MRID 42114819
Aerobic Soil Metabolism	Br <sub>2</sub> CA 23-26% at 14-30 days	—	—	MRID 41677404, 41677407
Anaerobic Soil Metabolism	Br <sub>2</sub> CA 49% by day 30, and remained at that level through day 90	—	—	MRID 42114821
Aerobic Aquatic Metabolism	—	—	α-R-deltamethrin - 24% at day 14	MRID 44977005
Terrestrial Field Dissipation	Br <sub>2</sub> CA 0.5 ppb at 4 days	—	—	MRID 42137505, 42773903, 42114822

It appears that 3-PBA (at high levels in the aerobic soil metabolism study) and 3-PBAldehyde are not very persistent in the environment (the latter was not measured in tralomethrin studies). However, Br<sub>2</sub>CA (observed in multiple studies) appears to persist much more than the former compounds. It was observed in laboratory studies and in the field (study conducted with deltamethrin). These degradates are the result of the ester rupture in the parent molecule. Other transformation products that were observed in various of the studies (particularly in photolysis studies) were the  $\alpha$ -R-deltamethrin and R-tralomethrin, isomers of deltamethrin and tralomethrin, respectively.

Based on batch equilibrium data, a major degradate, Br<sub>2</sub>CA or decamethrinic acid, appeared to be mobile (Freundlich K<sub>F</sub>'s <1, and K<sub>FOC</sub>'s=10.1-46.8, FAO classification) in 5 soils. In addition, for the degradate 3-PBA, K<sub>F</sub>'s were in the range of 0.7-2.7 while the K<sub>FOC</sub>'s were in the range of 51-288 (mobile to moderately mobile, FAO classification). Of these degradates, Br<sub>2</sub>CA has the potential to leach to subsurfaces, or to reach adjacent bodies of water via runoff events, most likely dissolved in the water.

#### 4. Receptors

##### 4.1. Aquatic and Terrestrial Effects

The receptor is the biological entity that is exposed to the stressor (EPA, 1998). Due to the outdoor uses of tralomethrin, the types of receptors that may be exposed include both aquatic and terrestrial receptors, such as birds, reptiles, mammals and freshwater and estuarine/ marine fish, non-target invertebrates and terrestrial and aquatic plants. Spray drift and runoff exposures are expected for all ground, aerial and ULV applications of

tralomethrin. Consistent with the process described in the Overview Document (EPA, 2004), this risk assessment uses a surrogate species approach in its evaluation of tralomethrin. Toxicological data generated from surrogate test species, which are intended to be representative of broad taxonomic groups, are used to extrapolate to potential effects on a variety of species (receptors) included under these taxonomic groupings.

In addition to registrant-submitted studies, available open literature will be used to evaluate the potential direct effects of tralomethrin (and deltamethrin) to the terrestrial and aquatic receptors identified in this section. This includes toxicity data on the technical grade active ingredient, and when available, formulated products.

The open literature studies will be identified through EPA's ECOTOX database (<http://cfpub.epa.gov/ecotox/>), which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The evaluation of data can also provide insight into the direct and indirect effects of tralomethrin (and its major degradate, deltamethrin) on biotic communities from loss of species that are sensitive to the chemical and from changes in structure and functional characteristics of the affected communities.

Tables 4.1 and 4.2 provide a summary of the taxonomic groups and the surrogate species tested to help understand potential acute ecological effects of pesticides to these non-target taxonomic groups. In addition, the table provides a preliminary overview of the potential acute toxicity of tralomethrin by providing the acute toxicity classifications.

### *Terrestrial Species*

The available toxicity data suggest that tralomethrin is practically nontoxic to birds on an acute basis. The  $LD_{50} > 2,510$  mg/kg bw for bobwhite quail (*Colinus virginianus*), with 30 percent mortality at the highest concentration tested (2,510 mg/kg bw) (MRID 00073629). No submitted acute oral toxicity data are available on any other avian species. In an eight-day dietary study with bobwhite quail, the  $LC_{50}=4,740$  mg/kg diet (MRID 00058848). Data were also submitted for the mallard (*Anas platyrhynchos*), but the study yielded a less sensitive  $LC_{50}$  of 7,735 mg/kg diet (MRID 00073630). A twenty-three week bobwhite quail chronic study resulted in a  $NOAEL < 100$  mg/kg diet for reproductive effects (MRID 00104682). At the 100 mg/kg diet level, a statistically significant 23 percent reduction in number of hatchlings from three-week embryos was observed. A twenty-eight week avian reproduction toxicity study with mallards (*Anas platyrhynchos*) (MRID 00094896) indicates that tralomethrin exposure can result in a reduction of percent live three-week embryos and eggshell thickness at levels as low as 300 mg/kg diet ( $NOAEL < 300$  mg/kg diet). The degradate deltamethrin has a similar avian acute toxicity profile, with a 96-hour  $LD_{50} > 2250$  mg/kg bw for the bobwhite quail (MRID 00158273) and an 8-day mallard dietary  $LC_{50} > 4640$  mg/kg diet (MRID 00060723). Deltamethrin showed no adverse effects to reproduction at the highest concentration tested (450 mg/kg diet) in the two one-generation chronic studies conducted on the bobwhite quail and mallard (MRIDs 42114808 and 42114809).

For mammalian toxicity, EFED will coordinate with HED to determine the most sensitive endpoints for acute and chronic studies. The metabolism of tralomethrin by the rat has been extensively studied by Cole, et al. (1982) and Bosch (1990). Tralomethrin is generally not detected in treated mammals or their excreta since it undergoes rapid and essentially complete debromination to form deltamethrin.

As expected for a registered insecticide, tralomethrin is highly toxic to terrestrial invertebrates. An acute contact study on honeybees (*Apis mellifera*) for tralomethrin produced an  $LD_{50} = 0.129 \mu\text{g a.i./bee}$  (MRID 00149743). The degradate deltamethrin is also highly toxic to honeybees, with an acute contact  $LD_{50} = 0.0015 \mu\text{g/L}$  (MRID 42114815).

Table 4.1 Summary of most sensitive endpoints from submitted terrestrial toxicity studies for tralomethrin.						
Species (common name)	Taxa Represented	End-point	Mean Concentration	Test Substance (% a.i.)	Citation MRID	Acute Toxicity Classification
<i>Colinus virginianus</i> (Bobwhite quail)	Birds, terrestrial-phase amphibians, and reptiles	LD <sub>50</sub>	3,171 mg/kg-bw	98.5	00073629	Practically nontoxic
		LC <sub>50</sub>	4,740 mg/kg-diet	98.5	00058848	Practically nontoxic
		NOAEC	<100 ppm	97.0	00104682	NA
		LOAEC	100 ppm <sup>1</sup>			
<i>Apis mellifera</i> (Honey bee)	Terrestrial invertebrates	LD <sub>50</sub>	0.129 µg/bee	95.0	00149743	Highly toxic

<sup>1</sup>Based on percent of normal hatchlings from three-week embryos.

### *Aquatic Species*

Tralomethrin is considered to be very highly toxic to the freshwater rainbow trout (*Oncorhynchus mykiss*) on an acute basis, with an estimated 96-hour LC<sub>50</sub> = 1.6 µg/L based on nominal concentrations (MRID 00058849). This study had 70 percent mortality at the lowest concentration tested (1.8 µg/L). Another rainbow trout study (MRID 00058850) resulted in an LC<sub>50</sub>=34.7 µg/L. Acute toxicity studies on bluegill resulted in an LC<sub>50</sub> range of 4.23 µg/L – 44.9 µg/L (MRIDs 00058851 and 00058852). Studies conducted with Scout EC gave a 96-hour LC<sub>50</sub> range from 23 µg/L to 52 µg/L for bluegill sunfish (EPA Accession Numbers 403579-12, 403580-12 and MRIDs 00058852, 00132755) Scout EC studies with rainbow trout resulted in an LC<sub>50</sub> range of 14 µg/L to 120 µg/L (EPA Accession Numbers 403579-13, 403580-12 and MRIDs 00058850 and 00132756. (Note: The percent active ingredient of the end use product for each of these studies is unclear at this time, and will need to be assessed). The degradate deltamethrin is also very highly toxic to freshwater fish, with a 96-hour LC<sub>50</sub> = 0.58 µg/L in the most sensitive acute test conducted on pumpkinseed sunfish (MRID 00060721).

In addition to the acute freshwater fish studies, two chronic studies were submitted, an early life and a life-cycle study. The chronic freshwater life cycle fish study resulted in a 60-day NOAEC=0.088 µg/L and LOAEC=0.18 µg/L for the fathead minnow (*Pimephales promelas*) based on egg production and larval survival (MRID 41860701). The early-life stage NOAEC=0.18 µg/L and a LOAEC=0.35 µg/L for a 35-day early life test based on effects to hatching and fry survival (MRID 00132762). Deltamethrin also exhibited toxic chronic effects to freshwater fish, with a NOAEC = 0.017 µg/L and LOAEC = 0.035 µg/L based on a 280-day test with fathead minnow (MRID 42786802).

Daphnids (*Daphnia magna*) are used as the representative species for freshwater invertebrates for both acute and chronic effects. Acute toxicity values for aquatic invertebrates suggest that tralomethrin is very highly toxic to freshwater invertebrates with a 48-hour  $EC_{50} = 0.039 \mu\text{g/L}$  based on nominal concentrations (MRID 00058863). In studies conducted with the formulated product, the 48-hr  $EC_{50}$  for daphnids ranged from  $2.2 \mu\text{g/L}$  to  $55 \mu\text{g/L}$  (EPA Accession Numbers 403579-14, 403580-14 and MRID 00132757) (Note: The percent active ingredient of the end use product for each of these studies is unclear at this time, and will need to be assessed). The degradate deltamethrin is also highly acutely toxic to daphnids, with a 48-hour  $EC_{50} = 0.11 \mu\text{g/L}$  (MRID 44928701). In a 21-day chronic toxicity test observing the effects of tralomethrin to the *Daphnia magna* life cycle, the  $NOAEC = 0.00044 \mu\text{g/L}$  and the  $LOAEC = 0.00090 \mu\text{g/L}$  based on mean-measured concentrations (MRID 00132761). The endpoints affected for this study were length and number of young produced per adult per reproduction day. In a daphnid chronic life-cycle test with deltamethrin, the  $NOAEC = 0.0041 \mu\text{g/L}$  and the  $LOAEC = 0.0089 \mu\text{g/L}$  based on adverse effects to growth and reproductive success (MRID 42114813).

Estuarine/marine fish are represented by the sheepshead minnow (*Cyprinodon variegatus*). An acute toxicity study (MRID 00094897) with tralomethrin technical resulted in  $LC_{50} = 2.48 \mu\text{g a.i./L}$ , indicating tralomethrin is highly toxic to estuarine/marine fish. No estuarine/marine fish acute study was available for tralomethrin TEP. The degradate deltamethrin is very highly toxic to the sheepshead minnow, with a 96-hour  $EC_{50} = 0.36 \mu\text{g/L}$  (MRID 42114811). No registrant-submitted chronic estuarine/marine fish study is available for tralomethrin or the degradate deltamethrin.

Acute toxicity of tralomethrin to estuarine/marine aquatic invertebrates is represented by the pink shrimp (*Penaeus duorarum*). An acute 96-hour toxicity study indicates that tralomethrin is very highly toxic to estuarine/marine invertebrates, with an  $LC_{50} = 0.845 \mu\text{g a.i./L}$  (MRID 00094898). Additionally, for a 48-hour acute toxicity test with the eastern oyster embryos (*Crassostrea virginica*), the  $EC_{50} = 1.6 \mu\text{g/L}$  (MRID 00132758). A chronic toxicity test was conducted with the mysid shrimp (*Mysidopsis bahia*) and indicates high toxicity to estuarine/marine organisms on a chronic basis. In a 28-day life cycle study, the  $NOAEC = 0.00051 \mu\text{g/L}$  and the  $LOAEC = 0.00093 \mu\text{g/L}$ , based on reductions in survival, dry weight and number of offspring (Accession #264510). No estuarine/marine fish acute study was available for tralomethrin TEP.

The degradate deltamethrin is also very highly toxic to estuarine/marine aquatic invertebrates. In an acute study with mysid shrimp, the 96-hour  $LC_{50} = 0.0017 \mu\text{g/L}$  (MRID 42114812). For the eastern oyster, the 96-hour  $EC_{50} = 12.0 \mu\text{g/L}$  based on effects to shell deposition (MRID 41651016). No chronic estuarine/marine study with estuarine/marine invertebrates has been submitted for deltamethrin.

An aquatic field study has been submitted for tralomethrin (Scout 3.0 EC). This study was conducted on a 0.12 acre freshwater pond. The study indicates that macroinvertebrate communities were acutely affected in many of the taxonomic families, including Libellulidae, Leptoceridae, and Chironomidae (MRID 41283901). There

appeared to be no difference between total numbers and weights of bluegill, due to high variability among the replicates. These conclusions are based on visual examination of the data, and statistical analysis will be conducted prior to the risk assessment.

#### Aquatic Studies with Tralomethrin and Deltamethrin Co-formulation

Six studies were submitted for the tralomethrin/deltamethrin co-formulated product, HR2900 or Striker EC (12.4% a.i. of tralomethrin and deltamethrin in approximately equal proportions). For freshwater fish, this co-formulated product has a 96-hour  $LC_{50}=1.5 \mu\text{g a.i./L}$  for bluegill sunfish (MRID 43073903) and a 96-hour  $LC_{50}=0.39 \mu\text{g a.i./L}$  for rainbow trout (MRID 43073904). The tralomethrin/deltamethrin co-formulation has a 48-hour  $EC_{50}$  of 0.18 for freshwater invertebrates, represented by *Daphnia magna* (MRID 43073905). For estuarine/marine fish represented by the sheepshead minnow, the acute 96-hour  $LC_{50}=0.49 \mu\text{g a.i./L}$  (MRID 43073906). Acute estuarine/marine invertebrate toxicity tests with mysids resulted in an  $LC_{50}=0.021 \mu\text{g a.i./L}$  (MRID 43073908) and  $LC_{50}<110 \mu\text{g a.i./L}$  for eastern oysters (no endpoint was established because greater than a 50% reduction occurred at the lowest dose tested) (MRID 43073907).

For these studies on the tralomethrin and deltamethrin co-formulation, some uncertainty exists regarding the degree of the effect that can be attributed to the formulation (inerts and ingredients other than the active) and which are a result of the combining the two active ingredients. It is important to note that these studies give lower acute toxicity endpoints than either technical active ingredient or single active ingredient formulation alone for freshwater fish.

**Table 4.2. Summary of most sensitive endpoints from submitted aquatic toxicity studies for tralomethrin.**

Species (common name)	Taxa Represented	End- point	Duration (hours)	Mean concentration ( $\mu\text{g a.i./L}$ )	Citation MRID	Acute Toxicity Classification
<i>Oncorhynchus mykiss</i> (Rainbow trout)	Freshwater fish and aquatic- phase amphibians	$LC_{50}$	96	1.6	00058849	Very highly toxic
<i>Pimephales promelas</i>		NOAEC	60 (days)	0.088	41860701	NA
(Fathead Minnow)		LOAEC		0.18		
<i>Daphnia magna</i> (Water Flea)	Freshwater Invertebrates	$EC_{50}$	48	0.039	00058863	Very highly toxic
		NOAEC	21 (days)	0.0044	00132761	NA
		LOAEC		0.0090		
<i>Cyprinodon variegatus</i> (Sheepshead minnow)	Estuarine/ Marine Fish	$LC_{50}$	96	2.5	00094897	Very highly toxic

**Table 4.2. Summary of most sensitive endpoints from submitted aquatic toxicity studies for tralomethrin.**

Species (common name)	Taxa Represented	End- point	Duration (hours)	Mean concentration ( $\mu\text{g a.i./L}$ )	Citation MRID	Acute Toxicity Classification
<i>Penaeus duorarum</i> (Pink shrimp)	Estuarine/ Marine Invertebrates	LC <sub>50</sub>	96	0.845	00094898	Very highly toxic
<i>Mysidopsis bahia</i>		NOAEC	28 (days)	0.00051	Accession #264510	NA
(Mysid shrimp)		LOAEC		0.00093		

### Plants

No acceptable registrant-submitted terrestrial or aquatic plant data are available to the Agency for tralomethrin and the degradate deltamethrin.

## 4.2. Incident Database Review

A preliminary review on August 11, 2009 of the Ecological Incident Information System (EIIS, version 2.1), which is maintained by the Agency's Office of Pesticide Programs, and the Avian Monitoring Information System (AIMS), which is maintained by the American Bird Conservancy, indicates one reported ecological incident associated with the use of tralomethrin and one reported incident for the degradate deltamethrin. These incidents are summarized in Table 4.3. This total excludes incidents classified as 'unlikely' and only includes those incidents with certainty categories of 'highly probable', and 'probable' and 'possible' (for EIIS) and 'certain', 'highly likely', 'likely', 'probable', and 'possible' (for AIMS). In the EIIS and AIMS databases, the "unlikely" category is used when a chemical is not likely to be responsible for the incident. For example, an 'unlikely' classification might be applied in situations where a given chemical is practically nontoxic to the category of organism killed and/or there is evidence that another pesticide or stressor likely caused the incident. Incidents classified as 'unlikely' the result of tralomethrin will not be included in this Problem Formulation or the ecological risk assessment conducted for Registration Review.

Tralomethrin was classified as a probable cause for an incident in 1994 involving phytotoxic effects to bushes near a residential application site (application rate and magnitude of injury unknown) (EIIS I007155-153). In the single incident reported for deltamethrin (Deltaguard GC 5SC), two other chemicals were also involved, imidacloprid and thiophanate-methyl. These chemicals were applied to a golf course, and runoff caused a fish kill of approximately 350 bullhead fish (*Ameiurus* sp). Deltamethrin was considered the probable cause of the incident, as it is much more toxic to fish than either imidacloprid and thiophanate-methyl. Residues of deltamethrin were detected in water collected at the incident site at 0.13 ppb. This incident was classified as a misuse (EIIS I015407-001).

**Table 4.3. Wildlife Incidents Associated with Tralomethrin and the degradate Deltamethrin.**

Chemical Name	Incident Number (Source)	Taxa Involved	Magnitude	Year	Location (County, State)	Use	Legality of Use	Certainty Category <sup>1</sup>	Residues	Other Chemicals Involved
Tralo-methrin	EIIS 1007155-153	Terrestrial plants	Not reported	1994	Worcester, MA	Home	Unknown	Probable	Not available	None
Delta-methrin	EIIS 1015407-001	Fish ( <i>Ameriurus</i> sp.)	350 individuals	2004	Allen, OH	Golf Course	Misuse	Probable	0.13 ppb in affected water	Imidacloprid and Thiophanate-methyl

<sup>1</sup>Incidents classified as 'unlikely' are excluded.

Although only a total of two incidents for tralomethrin and deltamethrin have been reported to the Agency, the absence of reported incidents should not be construed as the absence of incidents. Incident reports for non-target organisms typically provide information only on mortality events and plant damage incidents. Except for phytotoxic effects in terrestrial plants, sublethal effects for organisms such as reduced growth or impaired reproduction are rarely reported. EPA's changes in the registrant reporting requirements for incidents in 1998 may account for a reduced number of reported incidents. Registrants are now only required to submit detailed information on 'major' fish, wildlife, and plant incidents. Minor fish, wildlife, and plant incidents, as well as all other nontarget incidents, are generally reported aggregately and are not included in EIIS. In addition, there have been changes in state monitoring efforts due to lack of resources.

In the risk assessment, the incidents will be further evaluated to determine if the reported incidents represent current patterns of use for tralomethrin. Examples of additional considerations are mitigation (*e.g.*, reduced application rates), product cancellations, and changes in use patterns that have occurred since the date of the reported incidents.

Additionally, a quick search for tralomethrin and deltamethrin in the USGS NAWQA database indicates that they are not currently being monitored in surface waters or sediments. The recent studies conducted by Stout II, *et al.* 2009, Weston *et al.* 2005, and Amweg *et al.* 2006 (discussed in **Section 3.2**) are examples of the prevalent nature of synthetic pyrethroids and their potential to affect organisms in the benthos.

#### **4.3. Ecosystems Potentially at Risk**

Tralomethrin may be applied on five food or feed crops: broccoli, cotton, lettuce,

soybeans and sunflowers. In addition, tralomethrin has multiple non-crop uses. Thus, the ecosystems at risk may be extensive in scope, and as a result it may not be possible to identify specific ecosystems during the development of a baseline risk assessment. In general terms, terrestrial ecosystems potentially at risk due to the use of tralomethrin, could include the treated field and areas immediately adjacent to the treated field that may receive drift or runoff. Areas adjacent to the treated field could include cultivated fields, fencerows and hedgerows, meadows, fallow fields or grasslands, woodlands, riparian habitats and other uncultivated areas. Due to the persistence of tralomethrin residues (tralomethrin and deltamethrin), they are expected to drift and/ or runoff due to application to food and/ or feed crops (or non-crop uses), resulting in possible exposure to aquatic ecosystems. Aquatic ecosystems potentially at risk due to the use of tralomethrin include water bodies adjacent to, or down stream from, the treated field and might include impounded bodies such as ponds, lakes and reservoirs, or flowing waterways such as streams or rivers. For uses in coastal areas, potentially affected aquatic habitat also includes marine ecosystems and estuaries.

## **5. Assessment Endpoints**

Assessment endpoints are defined as “explicit expressions of the actual environmental value that is to be protected.” Defining an assessment endpoint involves two steps: 1) identifying the valued attributes of the environment that are considered to be at risk; and 2) operationally defining the assessment endpoint in terms of an ecological entity (*i.e.*, a community of fish and aquatic invertebrates) and its attributes (*i.e.*, survival and reproduction). Therefore, selection of the assessment endpoints is based on valued entities (*i.e.*, ecological receptors), the ecosystems potentially at risk, the migration pathways of pesticides, and the routes by which ecological receptors are exposed to pesticide-related contamination. The selection of clearly defined assessment endpoints is important because they provide direction and boundaries in the risk assessment for addressing risk management issues of concern. Changes to assessment endpoints are typically estimated from the available toxicity studies, which are used as the measures of effects to characterize potential ecological risks associated with exposure to pesticides, such as tralomethrin.

To estimate exposure concentrations, the ecological risk assessment considers a single application at the maximum application rate to fields that have vulnerable soils. The most sensitive toxicity endpoints are used from surrogate test species to estimate treatment-related direct effects on acute mortality and chronic reproductive, growth and survival assessment endpoints. Toxicity tests are intended to determine effects of pesticide exposure on birds, mammals, fish, terrestrial and aquatic invertebrates, and plants. These tests include short-term acute, sub-acute, and reproduction studies and are typically arranged in a hierarchical or tiered system that progresses from basic laboratory tests to applied field studies. The toxicity studies are used to evaluate the potential of a pesticide to cause adverse effects, to determine whether further testing is required, and to determine the need for precautionary label statements to minimize the potential adverse effects to non-target animals and plants.

An open literature search will be conducted to determine any relevant endpoints. The search will focus on survival, growth and reproductive effects for aquatic and terrestrial effects of tralomethrin and for its major degradate, deltamethrin. More sensitive endpoints from acceptable open literature studies will be included in this risk assessment.

## **6. Conceptual Model**

For a pesticide to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from a source to an ecological receptor. For an ecological pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure.

A conceptual model provides a written description and visual representation of the predicted relationships between tralomethrin, potential routes of exposure, and the predicted effects for the assessment endpoint. A conceptual model consists of two major components: risk hypothesis and a conceptual diagram (EPA, 1998).

### **6.1. Risk Hypothesis**

Risk hypotheses are specific assumptions about potential adverse effects (*i.e.*, changes in assessment endpoints) and may be based on theory and logic, empirical data, mathematical models, or probability models (EPA 1998). For this assessment, the risk is stressor-initiated, where the stressor is the release of tralomethrin into the environment, with the formation of deltamethrin, its major transformation product. The following risk hypothesis is presumed for this screening-level assessment:

*Tralomethrin, when used in accordance with registered labels, will likely lead to off-site movement of the compound via runoff, spray drift, and eroded soil leading to exposure of nontarget plants and animals. Based on information on environmental fate, mode of action, direct toxicity and potential indirect effects, EFED assumes that registered uses of tralomethrin have the potential to cause reduced survival, growth, and reproduction to non-target terrestrial and/or aquatic animals and plants.*

The conceptual model is a generic graphic depiction of the risk hypothesis. It includes the potential pesticide or stressor (tralomethrin) and its transformation product (deltamethrin) as an additional stressor. It also includes the source of the pesticide and/or transport pathways, exposure media, exposure point, biological receptor types, and attribute changes.

### **6.2. Conceptual Diagram**

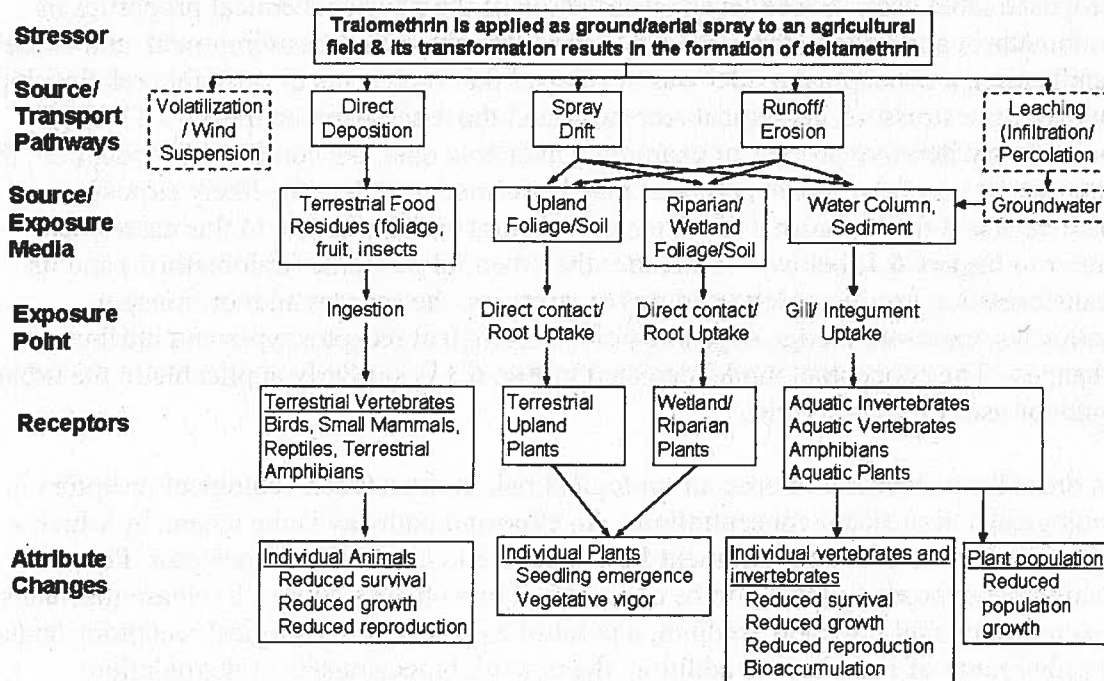
The conceptual site model is a generic graphic depiction of the risk hypothesis, and

assumes that the insecticide tralomethrin (and its transformation product, deltamethrin, another insecticide), having outdoor uses, is capable of affecting aquatic and terrestrial animals provided that environmental concentrations are sufficiently elevated as a result of proposed label uses. Based on an examination of the physicochemical properties of tralomethrin and deltamethrin, their fate and disposition in the environment, and mode of application, a conceptual model was developed that represents the possible relationships between the stressors, ecological receptors, and the assessment endpoints. Through a preliminary iterative process of examining available data, the conceptual model (*i.e.*, the representation of the risk hypothesis) may be refined to reflect the likely exposure pathways and the organisms that are most relevant and applicable to this assessment (refer to **Figure 6.1**, below). It includes the potential pesticide (tralomethrin) and its transformation product, (deltamethrin) or stressors, the sources and/ or transport pathways, exposure media, exposure points, biological receptor types and attribute changes. The conceptual model depicted in **Fig. 6.1** is similarly applicable to the urban outdoor uses of tralomethrin.

In order for a chemical to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from a source to an ecological receptor. For an ecological exposure pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure. In addition, the potential mechanisms of degradation/ transformation (*i.e.*, which degradation/ transformation products may form in the environment, in which media, and how much) must be understood, especially for a chemical whose metabolite/ transformation product could be of greater toxicological concern than the parent compound. The assessment of ecological exposure pathways, therefore, includes an examination of the source and potential migration pathways for constituents, and the determination of potential exposure routes.

Note: This simplified conceptual model does not show details about biomagnification for a chemical (though it shows bioaccumulation). Tralomethrin has a very high  $K_{ow}$  and according to its physicochemical and fate properties, there is a potential for bioaccumulation/ bioconcentration in aquatic organisms, and biomagnification in terrestrial organisms. The potential for bioaccumulation/ biomagnification is not stressed in this conceptual model, but will be examined in the risk assessment. See **Section 7.2 Measures of Exposure**.

**Figure 6.1. Ecological Conceptual Exposure Model for Screening-Level Risk Assessment of Tralomethrin Applied to Agricultural Fields**



Under the possible uses of tralomethrin, the sources and mechanisms of release of the compound are from ground or aerial spray applications, or ULV (it is noted that for non-agricultural uses, other methods of application may occur). Surface runoff from the areas of application is assumed to depend on factors such as topography, irrigation, and rainfall events. Direct deposition may result in contamination of food items that may be consumed by terrestrial organisms. Spray drift results in contaminated adjacent areas, such as bodies of water.

For aquatic receptors, the major point of exposure is through direct contact with the water column, sediment, and pore water (gill/ integument) contaminated with spray drift (from spray application) and/ or runoff from treated areas. Indirect effects to aquatic organisms (especially fish) can also occur through impact to various food chains and through bioaccumulation. The representative aquatic receptors are certain freshwater and estuarine/ marine fish, invertebrates, and, in certain cases, aquatic plants. The major point of exposure for terrestrial animals is consumption of food contaminated with residues such as grass, foliage, and small insects. For plants, the point of exposure is direct contact or root uptake. The representative terrestrial receptors are mammals, birds, and, in certain cases, terrestrial plants. The attribute changes used to assess risk terrestrial receptors depend on the type of test (e.g., reduced survival, growth, or reproduction for animals and seedling emergence and vegetative vigor for plants). It should be noted, that these species do not cover all the possible species in the animal and plant kingdoms; certain taxa are considered as surrogates for other taxa. For example,

fish are considered surrogates for aquatic phase amphibians.

## **7. Analysis Plan**

In order to address the risk hypothesis, the potential for adverse effects on the environment is estimated. Usage, environmental fate and transport, and ecological effects of tralomethrin are characterized and integrated to assess the risks. This is accomplished using a risk quotient (ratio of exposure concentration to effects concentration) approach. Although risk is often defined as the likelihood and magnitude of adverse ecological effects, the risk quotient-based approach does not provide a quantitative estimate of likelihood and/or magnitude of an adverse effect. However, as outlined in the Overview Document (USEPA 2004), the likelihood of effects to individual organisms from particular uses of a chemical is estimated using the probit dose-response slope and either the level of concern (discussed below) or the actual calculated risk quotient value.

This analysis plan will be revisited and may be revised depending upon the data available in the open literature and the information submitted by the public in response to the opening of the Registration Review docket.

### **7.1. Stressors of Concern**

The focus of this assessment is on the parent material, tralomethrin, and as noted below, its major transformation product, deltamethrin. The Agency will review open literature to identify degradate(s) of potential toxicological concern. One degradate of tralomethrin, deltamethrin, is structurally related to the parent compound, and is more persistent than the parent. In this assessment, only potential risk from deltamethrin as a degradate of tralomethrin will be addressed quantitatively, and the active ingredient deltamethrin will only be characterized qualitatively in the risk description.

Toxicity data for environmental mixtures of tralomethrin with other pesticides (those mixtures occurring in the environment following application), if available, may be presented as part of the ecological risk assessment. It is expected that the toxic effect of tralomethrin, in combination with other pesticides used in the environment, is likely to be a function of many factors including but not necessarily limited to: (1) the exposed species, (2) the co-contaminants in the mixture, (3) the ratio of tralomethrin and co-contaminant concentrations, (4) differences in the pattern and duration of exposure among contaminants, and (5) the differential effects of other physical/ chemical characteristics of the receiving waters (*e.g.* organic matter present in sediment and suspended water). Quantitatively predicting the combined effects of all these variables on mixture toxicity to any given taxa with confidence is beyond the capabilities of the available data and methodologies. However, a qualitative discussion of implications of the available pesticide mixture effects data on the confidence of risk assessment conclusions will be addressed as part of the uncertainty analysis.

### **7.2. Measures of Exposure**

In order to estimate risks of tralomethrin exposures in aquatic and terrestrial environments, all exposure modeling and resulting risk conclusions will be made based on maximum application rates for the current use patterns. Measures of exposure are based on aquatic and terrestrial models that predict estimated environmental concentrations (EECs) of tralomethrin and its degradate, deltamethrin, using maximum labeled application rates and methods, as well as any mitigation measures specifically indicated on the label. The models used to predict aquatic EECs are the Pesticide Root Zone Model coupled with the Exposure Analysis Model System (PRZM/EXAMS). The model used to predict terrestrial exposure is T-REX. The model used to derive EECs relevant to terrestrial and wetland plants is TerrPlant. The potential for bioaccumulation for the chemical is assessed using the model KABAM, as well as results from BCF studies. These models are parameterized using relevant registrant-submitted and reviewed environmental fate and transport data.

PRZM (v3.12.2, May 2005) and EXAMS (v2.98.4.6, April 2005) are screening simulation models coupled with the input shell PE5.pl (August, 2007) to generate daily exposures and 1-in-10 year EECs of tralomethrin plus its transformation products, that may occur from spray drift and runoff to surface water bodies adjacent to application sites. PRZM simulates pesticide application, movement and transformation on a field (agricultural or otherwise) and the resultant pesticide loadings to a receiving water body via runoff, erosion and spray drift. The EXAMS model simulates the fate of the pesticide and resulting concentrations in the water body. The standard scenario used for ecological pesticide assessments assumes application to a 10-hectare agricultural field that drains into an adjacent 1-hectare water body that is 2 meters deep (20,000 m<sup>3</sup> volume) with no outlet. PRZM/EXAMS is used to estimate screening-level exposure of aquatic organisms to tralomethrin and/ or deltamethrin. The measure of exposure for aquatic species is the 1-in-10 year return peak or rolling mean concentration. The 1-in-10 year peak is used for estimating acute exposures of direct effects to aquatic organisms. The 1-in-10-year 60-day mean is used for assessing chronic exposure to fish and aquatic-phase amphibians. The 1-in-10-year 21-day mean is used for assessing aquatic invertebrate chronic exposure.

Given the aquatic toxicity of tralomethrin and deltamethrin and their likelihood of occurring in sediment, the Agency will also consider the potential exposures resulting from benthic/ sediment concentrations (EECs). Pore water concentrations are commonly used to predict toxicity of non-ionic substances in sediments and characterize exposure to organisms that spend time in or near sediments (Di Toro *et al.* 1991; US EPA 2002). PRZM/EXAMS estimates 1-in-10-year peak, 21-day mean, and 60-day mean EECs for pore water.

Exposure estimates for terrestrial animals assumed to be in the target area are derived using the T-REX model (version 1.4.1, December 2008). For granular pesticides (not applicable for tralomethrin), this includes the amount of pesticide per square foot, used in LD50 per square foot risk assessment calculations. EECs for terrestrial plants inhabiting dry and wetland areas are derived using TerrPlant (version 1.2.2, 12/26/2006). This

model uses estimates of pesticides in runoff and in spray drift (assumed to be 0% for granulars) to calculate EECs. EECs are based upon solubility, application rate and minimum incorporation depth.

As indicated in **Section 2.3**, tralomethrin may have a potential to bioaccumulate/ bioconcentrate/ or biomagnify in terrestrial food chains. The potential for bioaccumulation of tralomethrin will also be examined in the risk assessment. Because tralomethrin has a high  $K_{ow}$  ( $1.19 \times 10^5$ ) and the chemical is persistent in sediments, there is a potential for bioaccumulation. The depuration rate is fairly high (half life of 6.4 days), but constant levels of exposure could potentially negate this factor (Laskowski, 2002; MRID 00152024). Bioaccumulation will be assessed using the results from BCF studies, as well as the  $K_{OW}$  Based Aquatic Bioaccumulation Model (KABAM, version 1.0, 2009), adjusting for biotransformation rates.

### **7.3. Measures of Effect**

Ecological effects data are used as measures of direct and indirect effects to biological receptors. Data are typically obtained from registrant-submitted studies or from literature studies identified by ECOTOX. The ECOTOX database provides more ecological effects data in an attempt to bridge existing data gaps. ECOTOX is a source for locating single chemical toxicity data and potential chemical mixture toxicity data for aquatic life, terrestrial plants, and wildlife. ECOTOX was created and is maintained by the USEPA, Office of Research and Development, and the National Health and Environmental Effects Research Laboratory's Mid-Continent Ecology Division.

Updated information on the potential effects of tralomethrin and the degradate deltamethrin on non-target organisms will also be collected from the Ecological Incident Information System (EIIS). The EIIS is a database containing adverse effect (typically mortality) reports on non-target organisms where such effects have been associated with the use of pesticides.

Where available, sub-lethal effects observed in both registrant-submitted and open literature studies will be evaluated qualitatively. Such effects may include behavioral changes (*e.g.*, lethargy and changes in coloration). Quantitative assessments of risks, though, are limited to those endpoints that can be directly linked to the Agency's assessment endpoints of impaired survival, growth and reproduction. Acute aquatic toxicity studies conducted with the Typical End-Use Product (TEP) may be used to assess effects as a result of exposure to spray drift only and only reflect potential effects from a brief exposure to the formulation.

The assessment of risk for direct effects to non-target organisms makes the assumption that the toxicity of tralomethrin to birds is similar to terrestrial-phase amphibians and reptiles. A similar assumption is made for fish and aquatic-phase amphibians.

The acute measures of effect used for animals in this assessment are the  $LD_{50}$ ,  $LC_{50}$  and  $EC_{50}$ . LD stands for "Lethal Dose", and  $LD_{50}$  is the amount of a material, given all at

once, that is estimated to cause the death of 50% of the test organisms. LC stands for “Lethal Concentration” and  $LC_{50}$  is the concentration of a chemical that is estimated to kill 50% of the test organisms. EC stands for “Effective Concentration” and the  $EC_{50}$  is the concentration of a chemical that is estimated to produce a specific effect in 50% of the test organisms. Endpoints for chronic measures of exposure for listed and non-listed animals are the NOAEL/NOAEC and NOEC. NOAEL stands for “No Observed-Adverse-Effect-Level” and refers to the highest tested dose of a substance that has been reported to have no harmful (adverse) effects on test organisms. The NOAEC (*i.e.*, “No-Observed-Adverse-Effect-Concentration”) is the highest test concentration at which none of the observed effects were statistically different from the control. The NOEC is the No-Observed-Effects-Concentration. For non-listed plants, only acute exposures are assessed (*i.e.*,  $EC_{25}$  for terrestrial plants and  $EC_{50}$  for aquatic plants); for listed plants either the NOAEC or  $EC_{05}$  is used.

#### **7.4. Integration of Exposure and Effects**

Risk characterization is the integration of exposure and ecological effects characterization to determine the potential ecological risk from the use of pesticides and the likelihood of direct and indirect effects to non-target organisms in aquatic and terrestrial habitats. The exposure and toxicity effects data are integrated in order to evaluate the risks of adverse ecological effects on non-target species. For the assessment of risks, the risk quotient (RQ) method is used to compare exposure and measured toxicity values. EECs are divided by acute and chronic toxicity values. The resulting RQs are then compared to the Agency’s Levels of Concern (LOCs) (USEPA 2004). These criteria will be used to indicate when tralomethrin’s uses, as directed on the label, have the potential to cause adverse direct or indirect effects to non-target organisms. In addition, incident data from the EIIS will be considered as part of the risk characterization.

#### **7.5. Deterministic and Probabilistic Assessment Methods**

The quantitative assessment of risk will primarily depend on the deterministic point-estimate based approach described in the risk assessment. An effort may also be made to further qualitatively describe risk using probabilistic tools that the Agency has developed. These tools have been reviewed by FIFRA Scientific Advisory Panels (<http://www.epa.gov/scipoly/sap/index.htm>) and have been deemed as appropriate means of refining assessments where deterministic approaches have identified risks.

#### **7.6. Endangered Species Assessments**

Consistent with the Agency’s responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to Federally-listed threatened and/or endangered (listed) species from registered uses of tralomethrin. This assessment will be conducted in accordance with the Overview Document (USEPA 2004), provisions of the ESA, and the Services’ *Endangered Species Consultation Handbook* (USFWS/NMFS, 1998).

The assessment of effects associated with the registration of tralomethrin is based on an

action area. The action area is considered to be the area directly or indirectly affected by the federal action, as indicated by the exceedance of Agency Levels of Concern (LOCs) used to evaluate direct or indirect effects. The Agency's approach to defining the action area under the provisions of the Overview Document (USEPA 2004) considers the results of the risk assessment process to establish boundaries for that action area with the understanding that exposures below the Agency's defined LOCs constitute a no-effect threshold. For the purposes of this assessment, attention will be focused on the footprint of the action (*i.e.*, the area where tralomethrin application occurs), plus all areas where offsite transport may result in potential exposure that exceeds the Agency's LOCs. Specific measures of ecological effect that define the action area for listed species include any direct and indirect effects and/ or potential modification of its critical habitat, including reduction in survival, growth, and reproduction as well as the full suite of sub-lethal effects available in the effects literature. Therefore, the action area extends to a point where environmental exposures are below any measured lethal or sub-lethal effect threshold for any biological entity at the whole organism, organ, tissue, and/ or cellular level of organization. In situations where it is not possible to determine the threshold for an observed effect, the action area is not spatially limited and is assumed to be the entire United States.

#### **7.7. Drinking Water Assessment**

A drinking water assessment will be conducted to support future human health risk assessments of tralomethrin if required. The drinking water assessment will incorporate model estimates of tralomethrin (and its transformation product, deltamethrin) in surface and ground waters. Concentrations in surface waters will be estimated using FQPA Index Reservoir Screening Tool (FIRST, v.1.1.1, 12/18/07) (or subsequently using PRZM/ EXAMS – see description above, if refinements are required). Ground water estimates of concentrations will be obtained using the Screening Concentration in Ground Water (SCI-GROW) model (v.2.3, July 2003). The drinking water assessment will also include a summary of available surface and ground water monitoring data.

#### **7.8. Preliminary Identification of Data Gaps**

##### **7.8.1. Fate**

Environmental fate data are requested for tralomethrin and for its major degradate deltamethrin. Deltamethrin will also be evaluated for registration review as a separate active ingredient (see Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review for Deltamethrin, USEPA, March 2010).

The environmental fate database for the parent compound **tralomethrin** is largely incomplete. The previous assessments of tralomethrin were based on early available studies. Later it was found that these studies did not follow current guidelines for testing pesticides. In addition, the assessments were done without the availability of aquatic metabolism studies, which are now being required. There are no recent assessments for the chemical, reason for which the data were not available. For registration review, the

following are the data gaps for the parent tralomethrin:

**835.2120 Hydrolysis** – The available study for tralomethrin was found to have several deficiencies, also, another study is available that greatly exceeds the solubility limit. Furthermore, the hydrolysis studies submitted more recently offered contradicting information, compared to the earlier studies. A new study is required.

**835.2240 Photodegradation in Water** – The available study for tralomethrin was found to have several deficiencies. The two available aqueous photolysis studies offer very different rates of reaction and high variability, and the extent and rate of reaction are uncertain. A new study is required.

**835.2410 Photodegradation on Soil** – The available study for tralomethrin was found to have several deficiencies. The soil photodegradation studies available offer very variable data between replicates and have various other deficiencies. The extent and rate of reaction are uncertain. A new study is required.

**835.4100 Aerobic Soil Metabolism** – One study for tralomethrin is available, that was conducted in one soil. A study must be conducted in three other soils to determine rates of transformation.

**835.4400 Anaerobic Aquatic Metabolism** – No study has been submitted for tralomethrin. The study is required.

**835.4300 Aerobic Aquatic Metabolism** – No study has been submitted for tralomethrin. The study is required.

**835.1230 Mobility Adsorption/ Desorption** – The registrant must clarify deficiencies observed in a previously submitted study (MRID 44814506), conducted on tralomethrin. Alternatively, a new study must be conducted.

**Environmental Chemistry Methods (ECMs) and Independent Laboratory Validations (ILVs) for Soil, Water and Sediment.** ECMs associated with the Terrestrial Field Dissipation study (Field dissipation §158.1300; OPPTS guidelines 835.6100, 835.6200, and 835.6300), along with successful confirmatory method trials (validation) by an independent laboratory (*i.e.* ILVs), are required. If there is risk concern for a given taxon, ECMs should be available for the environmental media in which organisms of the taxon reside. These ECMs should have limits of quantization for the residues of concern that are lower than the relevant toxicological levels of concern. All previous reviews on tralomethrin indicate that there is high concern for acute and chronic aquatic toxicity. Certain scenarios triggered acute and chronic levels of concern for aquatic invertebrates and chronic concerns for fish. In addition, the latter risk assessments conducted on deltamethrin, a major degradate of tralomethrin, indicated risk concerns for organisms living in freshwater and estuarine/ marine bodies of water. In addition, there were risk concerns for organisms living in the benthos. Therefore, ECMs for water and sediment are required in addition to the ECM for soil. The ECMs should

include parent and those residues found in the laboratory studies that exceeded 10% of the applied. The following appear to be the residues of concern for each media:

Soil – parent and major degradate, deltamethrin, and its epimers, *alpha*-R-deltamethrin, *trans*-deltamethrin, Br<sub>2</sub>CA, 3-PBAc

Water – parent and deltamethrin, and its epimers, *alpha*-R-deltamethrin, Br<sub>2</sub>CA, 3-PBAc, 3-PBAdehyde

Sediment – parent and deltamethrin, and its epimers, *alpha*-R-deltamethrin Br<sub>2</sub>CA, 3-PBAc and 3-PBAdehyde

The registrant is encouraged to submit state-of-the-art environmental chemistry methods; further, multi-residue methods (MRMs) for soil, water and sediment are preferred. The registrant submitted one method for soil and sediment (MRID 41283901, LOQ 10 ppb, published in the ECM website) for which the validation was carried out using only tralomethrin. The method states that it is capable of analyzing deltamethrin and *trans*-deltamethrin, but does not demonstrate or validate that claim (*i.e.* the method was not validated with deltamethrin). Also, the method cannot distinguish tralomethrin from deltamethrin. In addition, the registrant submitted a method for the combined residues of tralomethrin, deltamethrin and *trans*-deltamethrin in pond water. The method cannot distinguish between the same chemicals tested. One additional method (MRID 42773903, LOQ 2 ppb, published in the ECM website) is available, that could quantify deltamethrin, *trans*-deltamethrin and decamethrinic acid (Br<sub>2</sub>CA) in soil. A full description of the method validation procedures performed by an independent laboratory should be submitted. It should include the following information: (a) Recovery level(s) of the test compound(s) from the soil, water and sediment (substrates) at various relevant fortification level(s) using the residue analytical methodology; (b) a validated method sensitivity level; (c) results of the study and statistical test applied, including a stepwise presentation of the procedure for calculating percent recovery from the raw data; (d) all the data/ information necessary to independently verify the results; (e) summary of the results; and, (f) discussion and conclusions of the results.

The environmental fate database for the degradate **deltamethrin** is mostly complete. For registration review, the following are the data gaps for the chemical:

**835.4300. Aerobic Aquatic Metabolism** – A study is required for the degradate deltamethrin in one water/sediment system, which is preferably domestic since the supplemental data available is from two foreign water/ sediment systems (from the Neatherlands). The percent organic matter was very high in both sediments (3.0 and 12.4%), and furthermore, the pH of the water in both systems was above 8 (the range for two systems, measured at the initial and final intervals was 8.0 to 8.7). Deltamethrin is known to be susceptible to hydrolysis at higher pHs. The new test system should have a near neutral or slightly acidic pH. Also, other deficiencies included that the system was not completely aerobic or anaerobic, the analytical method could not distinguish deltamethrin from its primary  $\alpha$ -R-isomer or *trans*-deltamethrin, there is an unexplained steady decline in the material balance to 80-87% at the last test interval, and radioactive material may have been adhered to the walls of the vessels and the methodology could not account for that fact, as indicated in the study Data Evaluation Record (DER).

**835.4400. Anaerobic Aquatic Metabolism** – No study has been submitted for the degrade deltamethrin. The study is required.

**Environmental Chemistry Methods (ECMs), and Independent Laboratory Validations (ILVs), for Soil, Water and Sediment.** (See above, the applicable ECM and ILV requirement for the parent compound, tralomethrin.)

**Table 7.1** lists the status of the environmental fate data requirements for the parent compound, tralomethrin.

<b>Table 7.1. Summary of Environmental Fate Data Requirements for the Parent Tralomethrin</b>				
<b>Study Identification</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement?</b>	<b>Bibliographic Citation</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
<b>§158.1300 ENVIRONMENTAL FATE</b>				

**Degradation Studies-Lab:**

835.2120 Hydrolysis	1, 2	Yes	58862 & 58907; 44814501	Yes <sup>2</sup>
835.2240 Photodegradation In Water	1, 2	Yes	J. Agric. Food Chem. 29(4) 1981; 142904; 44814502	Yes <sup>2</sup>
835.2410 Photodegradation on Soil	1, 2	Yes	146120; 44814503	Yes <sup>2</sup>
835.2370 Photodegradation in Air	1, 2	No	NA	Waived <sup>3</sup>

**Metabolism Studies-Lab:**

835.4100 Aerobic Soil	1, 2	Yes	58859, 132549; 44814504	Yes <sup>4</sup>
835.4200 Anaerobic Soil	1, 2	Yes	132767 & 152021; 44814505	No
835.4400 Anaerobic Aquatic	1, 2	No	NA	Yes
835.4300 Aerobic Aquatic	1, 2	No	NA	Yes

**Mobility Studies:**

835.1230 Adsorption/ Desorption	1, 2	Yes	44814506	Yes <sup>5</sup>
835.1240 Leaching	1, 2	Yes	58860 & 132768	No
835.1410 Volatility (Lab)	1, 2	No	NA	Waived <sup>3</sup>
835.8100 Volatility (Field)	1, 2	No	NA	Waived <sup>3</sup>

<b>Table 7.1. Summary of Environmental Fate Data Requirements for the Parent Tralomethrin</b>				
<b>Study Identification</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement?</b>	<b>Bibliographic Citation</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>

**Dissipation Studies-Field:**

835.6100 Terrestrial Field Dissipation	1, 2	Yes	44814507, 44814508	No
835.6200 Aquatic Field Dissipation	1, 2	No	N/A	Reserved
835.6300 Forestry Dissipation	1, 2	No	N/A	N/A

**Ground Water Monitoring Studies:**

835.7100 Ground Water Monitoring	1, 2	No	NA	Reserved
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**§158.1100 SPRAY DRIFT**

840.1100 Spray Droplet Size Spectrum	1, 2	No <sup>2</sup>	NA	No <sup>6</sup>
840.1200 Spray Drift Field Deposition	1, 2	No <sup>2</sup>	NA	No <sup>6</sup>

**Other Studies:**

Environmental Chemistry Methods (ECM)	1, 2	Partially	41283901, 42773903	Yes <sup>7</sup>
Independent Laboratory Validation (ILV)	1, 2	No	NA	Yes <sup>7</sup>

1. Use Patterns: (1=Terrestrial/Food; 2=Terrestrial/Feed). 2. Studies available do not meet current guideline requirement, new studies are required. 3. Tralomethrin and its major degradate, deltamethrin have low vapor pressure and Henry's Law Constant. 4. A study must be conducted with three soil systems to determine rate and extent of reaction. 5. The registrant must clarify deficiencies observed in the DER dated 03/13/02 or conduct a new study. 6. Data requirement covered by submission of the Spray Drift Task Force. 7. The registrant is encouraged to submit state-of-the-art environmental chemistry methods; further, multi-residue methods (MRMs) for soil, water and sediment are preferred.

**Table 7.2** lists the status of the environmental fate data requirements for the major degradate deltamethrin.

**Table 7.2. Summary of Environmental Fate Data Requirements for the Degradate Deltamethrin**

Study Identification	Use Pattern <sup>1</sup>	Does EPA Have Data To Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
<b>§158.1300 ENVIRONMENTAL FATE</b>				

**Degradation Studies-Lab:**

835.2120 Hydrolysis	1,2	Yes	41651038	No
835.2240 Photodegradation in Water	1,2	Yes	42114818	No
835.2410 Photodegradation on Soil	1,2	Yes	42114819	No
835.2370 Photodegradation in Air	1,2	No	Not Available	Waived <sup>2</sup>

**Metabolism Studies-Lab:**

835.4100 Aerobic Soil	1,2	Yes	41677404, 41677407, 42114820	No
835.4200 Anaerobic Soil	1,2	Yes	42114821, 44814505	No
835.4400 Anaerobic Aquatic	1,2	No	Not Available	Yes
835.4300 Aerobic Aquatic	1,2	Partially	44977005	Yes <sup>3</sup>

**Mobility Studies:**

835.1230 Leaching – Adsorption/ Desorption	1,2	Yes	41651039, 42475908, 42976501, 44977006	No
835.1410 Volatility (Lab)	1,2	No	Not Available	Waived <sup>2</sup>
835.8100 Volatility (Field)	1,2	No	Not Available	Waived <sup>2</sup>

**Dissipation Studies-Field:**

835.6100 Terrestrial Field Dissipation	1,2	Yes	42114822, 42137505, 42773903	No
835.6200 Aquatic Field Dissipation	1,2	No	N/A	Reserved
835.6300 Forestry Dissipation	1,2	No	N/A	N/A

**Ground Water Monitoring Studies:**

**Table 7.2. Summary of Environmental Fate Data Requirements for the Degradate Deltamethrin**

Study Identification	Use Pattern <sup>1</sup>	Does EPA Have Data To Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
835.7100 Ground Water Monitoring	1,2	No	NA	Reserved
<b>§158.1100 SPRAY DRIFT</b>				
201-1 Droplet Size Spectrum	1,2	No <sup>2</sup>	NA	No <sup>4</sup>
202-1 Drift Field Evaluation	1,2	No <sup>2</sup>	NA	No <sup>4</sup>
<b>Other Studies:</b>				
ECM and ILV	1,2	Partially	42773903	Yes <sup>5</sup>

1. Use Patterns: 1=Terrestrial/Food; 2=Terrestrial/Feed. 2. Deltamethrin has low vapor pressure and Henry's Law Constant, data requirement was waived. 3. One study is required in only one water/sediment system. The system should be domestic, have a near neutral pH, and should address deficiencies listed in the previous study. 4. Data requirement covered by submission of the Spray Drift Task Force. 5. The registrant is encouraged to submit state-of-the-art environmental chemistry methods; further, multi-residue methods (MRMs) for soil, water and sediment are preferred.

### 7.8.2 Effects

Effects data is requested for tralomethrn and the degradate deltamethrin. Deltamethrin will also be evaluated for registration review as a separate active ingredient (see Environmental Fate and Ecological Risk Assessment Problem Formulation in Support of Registration Review for Deltamethrin, USEPA, March 2010). For registration review, the following data gaps exist for both tralomethrin and the degradate deltamethrin, unless otherwise specified:

#### **Guideline Number: 850-2100**

##### **Study Title: Passerine Acute Avian Oral**

Although an acute avian oral study was received the Agency updated its data requirements in 40 CFR Part 158 (October 26, 2007) to include an acute oral toxicity study for both a passerine species and either a waterfowl or an upland game species. Prior to starting toxicity testing, a protocol will need to be provided for review. Many passerine species utilize agricultural fields, forests, residential areas and surrounding areas, and, therefore, have the potential to be exposed to pesticides used in agricultural, forest, and residential settings. It is likely that, for most pesticide use patterns, passerines are more likely to be exposed to pesticides than upland game species and waterfowl. Passerines are smaller and have faster metabolisms than the waterfowl and upland game bird species traditionally used in avian toxicity tests which could impact their sensitivity to chemicals.

**Guideline Number: 850.1075**

**Study Title: Fish Acute Toxicity (saltwater, tralomethrin TEP only)**

**Guideline Number: 850.1025**

**Study Title: Oyster Acute Toxicity (saltwater, tralomethrin TEP only)**

**Guideline Number: 850.1035**

**Study Title: Mysid Acute Toxicity (saltwater, tralomethrin TEP only)**

Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas (see Fig. 3.1). Tralomethrin technical is highly toxic to estuarine/marine fish and invertebrates on an acute basis, but no information has been submitted for the tralomethrin TEP. A new study is required based on the absence of acceptable data to satisfy the guidelines for acute estuarine/marine fish and invertebrate studies with the typical end-use product.

**Guideline Number: 850.1400**

**Study Title: Fish Early Life-Stage (saltwater)**

**Guideline Number: 850.1500**

**Study Title: Fish Life Cycle (saltwater)**

Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas (see Fig. 3.1). Both tralomethrin and deltamethrin are highly toxic to estuarine/marine fish on an acute basis. A new study is required based on the absence of acceptable data to satisfy the guidelines for an early life stage and life cycle estuarine/marine fish studies. Chronic studies on estuarine/marine organisms are required to support uses by which significant concentrations of a chemical are expected to enter into estuarine/marine environments. Persistence in water (e.g., half-life in water >4 days) can also trigger this data requirement.

**Guideline Number: 850.1350**

**Study Title: Aquatic Invertebrate Life-Cycle (saltwater, deltamethrin only)**

The acute toxicity of the degradate deltamethrin to estuarine/marine invertebrates indicates the potential for chronic risk to animals in this taxon, and the potential for chronic exposure exists based on current usage patterns and available fate data. The parent compound tralomethrin exhibits chronic toxicity effects to estuarine/marine invertebrates. Without this study, the Agency would have to presume chronic risk to listed and non-listed estuarine/marine invertebrates, but would not be able to quantify the risk. The Agency had conditionally required fish early-life stage and aquatic invertebrate life-cycle studies (guidelines 850.1300, 850.1350, and 850.1400) for terrestrial food and nonfood, aquatic food and nonfood, forestry, and domestic outdoor uses.

**Guideline Number: 850-1790**

**Study Title: Whole sediment: chronic invertebrates freshwater and marine**

No chronic sediment toxicity tests for freshwater or marine invertebrates have been submitted to satisfy the Agency's updated data requirements for outdoor uses in 40 CFR Part 158 (October 26, 2007). Benthic organisms inhabit sediment environments that may be exposed to run-off or spray drift from tralomethrin applications used in agricultural,

forest, and residential settings. Previous studies have identified a potential adverse effect for freshwater and estuarine/marine aquatic organisms based on water column toxicity values. Therefore, there is uncertainty associated with that estimate that can be reduced using data from a toxicity test with benthic organisms. There is the potential for persistent exposure from tralomethrin and deltamethrin in sediment indicated by the fate properties and open literature studies on pyrethroids (Stout II, *et al.* 2009, Weston *et al.* 2005, and Amweg *et al.* 2006). For sediment studies involving pyrethroids, tests on *Hyaella azteca*, *Chironomus tentans*, and *Leptocheirus plumulosus* are requested. Although both are freshwater species, *Hyaella* and *Chironomus* differ substantially in their ecological niche (i.e., epibenthic vs. infaunal species), physiology, and there is some evidence suggesting *Hyaella* is among the more sensitive invertebrates to some pyrethroids based on water column tests (Anderson *et al.* 2006).

**Guideline Numbers: 850.4150 and 850.4250**

**Study Title: Vegetative vigor and Seedling emergence, Tier I/ Tier II**

No acceptable toxicity data are currently available to assess the risk of tralomethrin and the degradate deltamethrin to terrestrial plants. Since tralomethrin has residential outdoor uses, vegetative vigor and seedling emergence studies are required. These phytotoxicity data are needed to evaluate the level of pesticide exposure to non-target terrestrial and aquatic plants and to assess the impact of pesticides on endangered and threatened plants.

**Guideline Number: 850.4400**

**Study Title: Aquatic Vascular Plant Growth-*Lemna* spp. Tiers I/II**

No acceptable studies for tralomethrin and the degradate deltamethrin have been submitted for vascular aquatic plants. The Agency has finalized its update to the data requirements in 40 CFR Part 158. In these updated data requirements, which were promulgated on October 26, 2007, vascular plant testing is required for pesticides such as tralomethrin with outdoor uses.

**Guideline Number: 850.5400**

**Study Title: Algal toxicity test, Tier I/II**

No toxicity data are currently available to assess the risk of tralomethrin and the degradate deltamethrin to aquatic nonvascular plants. Since tralomethrin has residential outdoor uses, Tier I/II aquatic nonvascular plant studies are required. These phytotoxicity data are needed to evaluate the level of pesticide exposure to non-target aquatic plants and to assess the impact of pesticides on endangered and threatened plants.

For mammalian toxicity, EFED will coordinate with HED to determine the most sensitive endpoints for acute and chronic studies.

*Testing on Typical end-use products (TEP)*

According to the Part 158 data requirements, testing on the typical end-use product may be required for aquatic toxicity tests when any of the following conditions exist:

1. The end-use product will be introduced directly into the aquatic environment.
2. The maximum expected environmental concentration or estimated

environmental concentration in the aquatic environment is greater than or equal to one-half the LC<sub>50</sub> or EC<sub>50</sub> of the TGAI.

3. An ingredient in the end-use formulation other than the active ingredient is expected to enhance the toxicity of the active ingredient or cause toxicity to aquatic organisms.

Previous assessments on tralomethrin indicate that the expected environmental concentrations in aquatic environments are well above acute 50% mortality levels for all species tested. For example, the maximum aquatic EEC was 13.94 µg/L in the cotton and tomato assessments. In estuarine/marine tests conducted with tralomethrin technical, the lowest 96-hour LC<sub>50</sub> was 2.5 µg/L for sheepshead minnow and 0.845 µg/L for pink shrimp. Therefore, tralomethrin fulfills the second requirement for TEP testing with estuarine/marine species.

A Typical End-Use Product is defined in the *Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Nontarget plants* on Part 120-2(1) on Page 18 as “a pesticide product that is representative of a major formulation category (e.g., emulsifiable concentrate, granular product, wettable powder) and pesticide group (e.g., herbicide, fungicide, insecticide etc.) and contains the active ingredient of the applicant’s product.” (Holst and Ellwanger, 1982)

Page 5 of the *Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Nontarget plants* provides additional information on what TEP data should be tested for toxicity testing in the following excerpt.

“The Agency seeks to avoid imposing a burden of duplicative testing on applicants for registration. Therefore, where 40 CFR Part 158 specifies that the test substance should be a representative end-use product, testing may be performed using the formulation in question (end-use product being registered) or similar, yet representative, end-use product. It is not necessary to repeat the test using other similar products.” (Holst and Ellwanger, 1982).

When TEP data are requested data should be submitted for the different formulations, e.g., wettable powder, emulsifiable concentrate, granular, along with a rationale as to why the TEP is representative of other similar end-use products. Acute aquatic toxicity studies conducted with the Typical End-Use Product (TEP) may be used to assess effects as a result of exposure to spray drift only and reflect potential effects from a brief exposure to the formulation. Therefore, appropriate TEPs should be selected from formulations that are registered for agricultural uses, not residential.

**Table 7.3. Ecological Effects Data Requirements for Tralomethrin\***

<b>Data Requirement</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)</b>	<b>Bibliographic Citation (MRID)</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
<b>§158.490 WILDLIFE AND AQUATIC ORGANISMS</b>				
<b>71-1(a) Acute Avian Oral, Quail/Duck/Passerine</b>	<b>1, 2</b>	<b>Partially</b>	<b>00073629</b>	<b>Yes, passerine study</b>
71-2(a) Acute Avian Diet, Quail	1, 2	Yes	00058848	No
71-2(b) Acute Avian Diet, Duck	1, 2	Yes	00073630	No
71-3 Wild Mammal Toxicity	1, 2		NA	
71-4(a) Avian Reproduction Quail	1, 2	Yes	00104682	No
71-4(b) Avian Reproduction Duck	1, 2	Yes	00094896	No
71-5(a) Simulated Terrestrial Field Study	1, 2		NA	
71-5(b) Actual Terrestrial Field Study	1, 2		NA	
72-1(a) Acute Fish Toxicity Bluegill	1, 2	Yes	00058851	No
72-1(b) Acute Fish Toxicity (TEP)	1, 2	Yes	00132755	No
72-1(c) Acute Fish Toxicity Rainbow Trout	1, 2	Yes	00058849	No
72-1(d) Acute Fish Toxicity Rainbow Trout (TEP)	1, 2	Yes	00132756	No
72-2(a) Acute Aquatic Invertebrate	1, 2	Yes	00058863	No
72-2(b) Acute Aquatic Invertebrate (TEP)	1, 2	Yes	00132757	No
72-3(a) Acute Est/Mar Toxicity Fish	1, 2	Yes	00094897	No
72-3(b) Acute Est/Mar Toxicity Mollusk	1, 2	Yes	00132758	No
72-3(c) Acute Est/Mar Toxicity Shrimp	1, 2	Yes	00094898	No
<b>72-3(d) Acute Est/Mar Toxicity Fish (TEP)</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>72-3(e) Acute Est/Mar Toxicity Mollusk (TEP)</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>72-3(f) Acute Est/Mar Toxicity Shrimp (TEP)</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>72-4(a) Early Life Stage Fish</b>	<b>1, 2</b>	<b>Partially</b>	<b>NA</b>	<b>Yes<sup>1</sup></b>
72-4(b) Life Cycle Aquatic Invertebrate	1, 2	Yes	00132761, 00162969	No

**Table 7.3. Ecological Effects Data Requirements for Tralomethrin\***

<b>Data Requirement</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)</b>	<b>Bibliographic Citation (MRID)</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
<b>72-5 Life Cycle Fish</b>	<b>1, 2</b>	<b>Partially</b>	<b>NA</b>	<b>Yes<sup>2</sup></b>
<b>72-6 Aquatic Organism Accumulation</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>72-7(1) Simulated Aquatic Field Study</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>72-7(b) Actual Aquatic Field Study</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>Whole sediment: acute freshwater invertebrates</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>Whole sediment: acute marine invertebrates</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>Whole sediment: chronic invertebrates freshwater &amp; marine</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>§158.540 PLANT PROTECTION</b>				
<b>122-1(a) Seed Germ, Seedling Emergence</b>	<b>1,2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>122-1(b) Vegetative Vigor</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>122-2 Aquatic Plant Growth</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes<sup>3</sup></b>
<b>124-1 Terrestrial Field Study</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>124-2 Aquatic Field Study</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>§158.490 NONTARGET INSECT TESTING</b>				
<b>141-1 Honey Bee Acute Contact</b>	<b>1, 2</b>	<b>Yes</b>	<b>00149743</b>	<b>No</b>
<b>141-2 Honey Bee Residue on Foliage</b>	<b>1, 2</b>	<b>Yes</b>	<b>00132764</b>	<b>No</b>
<b>141-5 Field Test for Pollinators</b>	<b>1, 2</b>		<b>NA</b>	
<b>§158.630 AQUATIC ORGANISMS TESTING</b>				
<b>850.1730 Bioaccumulation in Fish</b>	<b>1, 2</b>	<b>Yes</b>	<b>152024</b>	<b>No</b>

<sup>1</sup> Use Patterns: (1=Terrestrial/Food; 2=Terrestrial/Feed).

<sup>2</sup> Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas (see Fig. 3.1). Tralomethrin is highly toxic to estuarine/marine fish and invertebrates on an acute basis.

<sup>3</sup> Aquatic toxicity tests are required for both algal and aquatic vascular species.

**Table 7.4. Ecological Effects Data Requirements for the Degradate Deltamethrin**

<b>Data Requirement</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)</b>	<b>Bibliographic Citation</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
<b>§158.490 TERRESTRIAL ORGANISMS</b>				
71-1(a) Acute Avian Oral, Quail/Duck	1,2	Partially	00158273	Yes <sup>2</sup>
71-2(a) Acute Avian Diet, Quail	1,2	No	NA	Waived <sup>3</sup>
71-2(b) Acute Avian Diet, Duck	1,2	Yes	00060723	No
71-3 Wild Mammal Toxicity	1,2		NA	
71-4(a) Avian Reproduction Quail	1,2	Yes	42114808	No
71-4(b) Avian Reproduction Duck	1,2	Yes	42114809	No
71-5(a) Simulated Terrestrial Field Study	1,2		NA	
71-5(b) Actual Terrestrial Field Study	1,2		NA	
<b>§158.630 AQUATIC ORGANISMS TESTING</b>				
72-1(a) Acute Fish Toxicity Bluegill	1,2	Yes	00158275	No
72-1(b) Acute Fish Toxicity (TEP)	1,2	Yes	41651013	No <sup>4</sup>
72-1(c) Acute Fish Toxicity Rainbow Trout	1,2	Yes	00158274	No
72-2(a) Acute Aquatic Invertebrate	1,2	Yes	44928701	No
72-2(b) Acute Aquatic Invertebrate (TEP)	1,2	Yes	41651014	No
72-3(a) Acute Est/Mar Toxicity Fish	1,2	Yes	41651015	No
72-3(b) Acute Est/Mar Toxicity Mollusk	1,2	Yes	41651016	No
72-3(c) Acute Est/Mar Toxicity Shrimp	1,2	Yes	42114810	No
72-3(d) Acute Est/Mar Toxicity Fish (TEP)	1,2	Yes	42114811	No
72-3(e) Acute Est/Mar Toxicity Mollusk (TEP)	1,2	Yes	41651017	No
72-3(f) Acute Est/Mar Toxicity Shrimp (TEP)	1,2	Yes	42114812	No
72-4(a) Early Life Stage Fish	1,2	Partially	42114814	Yes <sup>5</sup>
72-4(b) Life Cycle Aquatic Invertebrate (freshwater)	1,2	Yes	42114813	No

**Table 7.4. Ecological Effects Data Requirements for the Degradate Deltamethrin**

<b>Data Requirement</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)</b>	<b>Bibliographic Citation</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
<b>850.1350 Life Cycle Aquatic Invertebrate (saltwater)</b>	<b>1,2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>72-5 Life Cycle Fish</b>	<b>1,2</b>	<b>Partially</b>	<b>42786802</b>	<b>Yes<sup>5</sup></b>
<b>72-6 Aquatic Organism Accumulation</b>	<b>1,2</b>		<b>NA</b>	
<b>72-7(1) Simulated Aquatic Field Study</b>	<b>1,2</b>		<b>NA</b>	
<b>72-7(b) Actual Aquatic Field Study</b>	<b>1,2</b>		<b>NA</b>	
<b>850.1730 Bioaccumulation in Fish</b>	<b>1,2</b>	<b>Yes</b>	<b>41651040, 43072701, 43072702</b>	<b>No</b>
<b>850.1735 Whole sediment: acute freshwater invertebrates</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>850.1740 Whole sediment: acute marine invertebrates</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>No</b>
<b>Whole sediment: chronic invertebrates freshwater &amp; marine</b>	<b>1, 2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>§158.540 PLANT PROTECTION</b>				
<b>122-1(a) Seed Germ, Seedling Emergence</b>	<b>1,2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>122-1(b) Vegetative Vigor</b>	<b>1,2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>122-2 Aquatic Plant Growth</b>	<b>1,2</b>	<b>No</b>	<b>NA</b>	<b>Yes</b>
<b>123-1(a) Seed Germ./Seedling Emerg.</b>	<b>1,2</b>	<b>NA</b>	<b>NA</b>	<b>No<sup>7</sup></b>
<b>123-1(b) Vegetative Vigor</b>	<b>1,2</b>	<b>NA</b>	<b>NA</b>	<b>No<sup>7</sup></b>
<b>123-2 Aquatic Plant Growth</b>	<b>1,2</b>	<b>NA</b>	<b>NA</b>	<b>No<sup>8</sup></b>
<b>124-1 Terrestrial Field Study</b>	<b>1,2</b>		<b>NA</b>	
<b>124-2 Aquatic Field Study</b>	<b>1,2</b>		<b>NA</b>	
<b>§158.490 NONTARGET INSECT TESTING</b>				
<b>141-1 Honey Bee Acute Contact</b>	<b>1,2</b>	<b>Yes</b>	<b>42114815</b>	<b>No</b>
<b>141-2 Honey Bee Residue on Foliage</b>	<b>1,2</b>	<b>Yes</b>	<b>42475905 and 42773902</b>	<b>No</b>
<b>141-5 Field Test for Pollinators</b>	<b>1,2</b>		<b>NA</b>	

**Table 7.4. Ecological Effects Data Requirements for the Degradate Deltamethrin**

<b>Data Requirement</b>	<b>Use Pattern<sup>1</sup></b>	<b>Does EPA Have Data To Satisfy This Requirement? (Yes, No, or Partially)</b>	<b>Bibliographic Citation</b>	<b>Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?</b>
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<sup>1</sup> Use Patterns: 1=Terrestrial/Food; 2=Terrestrial/Feed.

<sup>2</sup> Data are required for one passerine species and either on waterfowl or one upland game bird species. At this time, only an acute oral test for a game bird species has been submitted.

<sup>3</sup> Because none of the previously submitted studies show any acute oral, dietary or chronic toxic effects to waterfowl and upland game bird species, no dietary study is required for the mallard duck.

<sup>4</sup> Part 158 data requirements state that the freshwater fish test species for the TEP testing should be the most sensitive of the species tested with the TGAI. The 96-hour LC<sub>50</sub> = 0.91 µg a.i./L for coldwater rainbow trout (*Oncorhynchus mykiss*) and warmwater bluegill sunfish (*Lepomis macrochirus*) (MRIDs 00158274 and 00158275) were equivalent for deltamethrin technical. The most sensitive species tested for deltamethrin technical acute toxicity was *Lepomis gibbosus* (Pumpkinseed sunfish) (MRID 00060721). However *Lepomis gibbosus* is not a guideline species. Therefore, the rainbow trout acute toxicity test for the formulated product satisfies the guideline requirement.

<sup>5</sup> Data are required for saltwater/marine fish species. With current registered use patterns, deltamethrin can potentially enter water bodies, based on the available environmental fate data. Exposure to aquatic organisms is also evidenced by studies from Weston *et al* (2005) and Amweg *et al* (2006). Furthermore, the acute LC<sub>50</sub> = 0.36 µg a.i./L for estuarine/marine fish, indicating that deltamethrin is very highly toxic on an acute basis to sheepshead minnow (MRID 42114811). Available ecological studies also show that low-level chronic exposure to deltamethrin has the potential to cause adverse reproductive effects in freshwater fish (NOAEC = 0.017 µg a.i./L, MRID 42786802).

<sup>6</sup> Aquatic toxicity tests are required for both algal and aquatic vascular species.

<sup>7</sup> Required if a tested terrestrial species exhibits a 25 percent or greater detrimental effect in the Tier I study.

<sup>8</sup> Required if a tested aquatic species exhibits a 50 percent or greater detrimental effect in a Tier I study.

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## **Appendix A. SRRD data request justification tables**

The following proposed Data Call-In tables include rationales for requiring the data requested in this problem formulation, explanations of the utility of the data, and explanations for how the data might impact risk assessment, following the format provided by SRRD.

**For the parent compound tralomethrin:**

**Guideline Number: 835.2120**

**Study Title: Hydrolysis**

**Guideline Number: 835.2240**

**Study Title: Photodegradation in Water**

**Guideline Number: 835.2410**

**Study Title: Photodegradation on Soil**

**Guideline Number: 835.4400**

**Study Title: Anaerobic Aquatic Metabolism**

**Guideline Number: 835.4300**

**Study Title: Aerobic Aquatic Metabolism**

**Rationale for Requiring the Data**

According to 40 CFR Part 158, Subpart N (Environmental Fate) §158.1300 (Environmental fate data requirements table), these data are required for all terrestrial use patterns. The Agency has no valid studies to rely on. One previous hydrolysis study was conducted at a concentration that greatly exceeded the solubility limit and another had various other deficiencies. The two available aqueous photolysis studies offer very different rates of reaction and high variability, and the rate and extent of reaction are not clear. The soil photodegradation studies available offer very variable data between replicates and have various other deficiencies. There are no aquatic metabolism studies (aerobic or anaerobic).

Furthermore, the hydrolysis and aqueous photolysis studies submitted more recently offered contradicting information, compared to the earlier studies.

**Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

The previous assessments were based on early available studies. Later it was found that these studies did not follow current guidelines for testing pesticides. In addition, the assessments were done without the availability of aquatic metabolism studies. There are no recent assessments for the chemical.

**How will the data be used?**

Tralomethrin is a synthetic pyrethroid with high toxicity towards aquatic organisms, including those living in the benthos. Knowledge of its persistence in aquatic and soil environments and upon irradiation is important. The results of these studies will be used in the environmental fate assessment, and later on, in the ecological risk characterization.

The data on rate of hydrolysis, aqueous photolysis, and aerobic and anaerobic aquatic metabolism are directly needed in the aquatic models GENEEC2, PRZM/ EXAMS and FIRST. The results from these models are used for ecological risk estimation and in drinking water exposure assessments.

**How could the data impact the Agency's future decision-making?**

Without these data, the Agency would have to make certain conservative assumptions (e.g. assume that tralomethrin is stable to aqueous photolysis when it is known that it degrades mostly

to deltamethrin). These conservative assumptions could lead to higher and inaccurate predicted concentrations (EECs), according to the models, and consequently, higher risk quotients. Also, a high degree of uncertainty could occur because, upon most of the transformation routes, tralomethrin degrades to deltamethrin, another synthetic pyrethroid insecticide with other toxicological and fate profiles. Knowledge of these dissipation pathways in detail is essential to perform a better and accurate environmental fate assessment and risk assessment.

The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin that may be unnecessary.

**For the parent compound tralomethrin**

**Guideline Number: 835.4100**

**Study Title: Aerobic Soil Metabolism**

**Guideline Number: 835.1230**

**Study Title: Mobility – Adsorption/ Desorption**

**Rationale for Requiring the Data**

According to 40 CFR Part 158, Subpart N (Environmental Fate) §158.1300 (Environmental fate data requirements table), these data are required for all terrestrial use patterns.

The Agency has only one aerobic soil metabolism study, conducted in one soil. According to current guidelines, three other soils should be tested in order to determine rates of transformation.

Additional data on adsorption-desorption are needed because it appears that in the available study the test compound was not stable following the adsorption and desorption phases. The deficiencies of the study should be addressed or a new study should be conducted.

**Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

Rates of dissipation of tralomethrin were calculated using the formation of  $^{14}\text{CO}_2$ ; while this information provided qualitative information about the disappearance of the chemical, it does not distinguish tralomethrin from deltamethrin or other degradation products.

The mobility was previously assessed, based on early available studies that used soil TLC and soil columns. These studies do not follow more current guidelines for testing pesticides.

There are no recent assessments for the chemical that used the newly submitted studies.

**How will the data be used?**

There is one aerobic soil metabolism study conducted with one soil that provides information on the nature of tralomethrin degradates. The new studies will provide additional information on the rate of reaction that will be used for environmental fate assessment, ecological risk characterization.

In addition, the data will be used to derive the rate of reaction input parameter to be used in the aquatic models GENEEC2, PRZM/ EXAMS, FIRST and SCI-GROW. The results from these models are used for ecological risk estimation and in drinking water exposure assessments.

**How could the data impact the Agency's future decision-making?**

Without these data, the Agency would have to make certain conservative assumptions (e.g. use a three times the aerobic soil metabolism half-life as input parameter in the aquatic models). These conservative assumptions could lead to higher (or lower) predicted concentrations, according to the models, and consequently, higher risk quotients. Also, there would be a high degree of uncertainty in the environmental fate assessment.

The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin that may be unnecessary.

**For the major degradate deltamethrin:**

**Guideline Number: 835.4300**

**Study Title: Aerobic Aquatic Metabolism**

**Guideline Number: 835.4400**

**Study Title: Anaerobic Aquatic Metabolism**

#### **Rationale for Requiring the Data**

According to 40 CFR Part 158, Subpart N (Environmental Fate) §158.1300 (Environmental fate data requirements table), these data are required for all terrestrial use patterns.

An aerobic aquatic metabolism study is required in one water/sediment system, which is preferably domestic since the supplemental data available is from two foreign water/ sediment systems. The percent organic matter was very high in both sediments (3.0 and 12.4%), and furthermore, the pH of the water in both systems was above 8 (range for two systems, measured at the initial and final intervals was pH of 8.0 to 8.7). Deltamethrin is known to be susceptible to hydrolysis at higher pHs. The new test system should have a near neutral pH. Also, other deficiencies listed in the study Data Evaluation Record (DER) should be addressed.

There is no anaerobic aquatic metabolism study.

#### **Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

The previous assessments were based on supplemental aerobic aquatic metabolism data and the anaerobic soil metabolism study.

**How will the data be used?**

Deltamethrin is a synthetic pyrethroid with high toxicity towards aquatic organisms, including those living in the benthos. Knowledge of its persistence in aquatic environments is important. The results of this study will be used in the environmental fate assessment, and later on, in the ecological risk characterization.

In addition, the data will be used to derive the rate of reaction input parameter to be used in the aquatic models GENEEC2, PRZM/ EXAMS and FIRST. The results from these models are used for ecological risk estimation and in drinking water exposure assessments.

**How could the data impact the Agency's future decision-making?**

Without these data, the Agency would have to make certain conservative assumptions (e.g. use a two times the aerobic soil metabolism half-life input for the aerobic aquatic metabolism or two times the anaerobic soil metabolism half-life for the anaerobic aquatic metabolism in the aquatic models). These conservative assumptions could lead to higher predicted concentrations (EECs), according to the models, and consequently, higher risk quotients. Also, there would be a higher degree of uncertainty in the environmental fate assessment. Knowledge of these dissipation pathways in detail is essential to perform a better and accurate environmental fate assessment and risk assessment.

The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for deltamethrin that may be unnecessary.

**For the parent compound tralomethrin, including its major degradate deltamethrin:**

**Guideline Number: None**

**Study Title: Environmental Chemistry Methods (ECM) and Independent Laboratory Validation (ILV) for Soil, Water and Sediment**

**Rationale for Requiring the Data**

According to the data requirements in 40 CFR Part 158, ECMs are currently required along with successful confirmatory method trials (validation) by an independent laboratory (*i.e.* ILVs). In addition to the method for soil, at this time, methods are required for water and sediment. Acceptable ECMs for the residues of concern (parent and its transformation products) should have levels of quantization that are adequate to address risk concerns or that are at levels below the toxicological endpoints for the relevant aquatic organisms. The results of previous assessments indicate that there is risk for freshwater and estuarine/ marine fish, invertebrates and benthic organisms. Therefore, ECMs for water and sediment are required in addition to the ECM for soil. The ECMs should include parent and those residues found in the laboratory studies that exceeded 10% of the applied. The registrant is encouraged to submit state-of-the-art environmental chemistry methods; further, multi-residue methods (MRMs) for soil, water and sediment are preferred.

**Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

Instead of monitoring data, models were utilized to calculate the exposure (*i.e.* Estimated Environmental Concentrations, EECs), using available environmental fate data. Currently, there is a published method for soils and sediments, but it is unable to distinguish tralomethrin from deltamethrin (<http://www.epa.gov/oppbead1/methods/ecminindex.htm>).

**How will the data be used?**

The data will be used to verify the suitability of the methods. Subsequently the methods could be used by states or other enforcement agencies, departments or entities, to monitor concentrations of the residues of concern. Validated analytical methods in environmental media (*a.k.a.*, ECMs) are useful for conducting and evaluating submitted environmental fate and toxicity field and monitoring studies and for addressing potential risks to the environment posed by the use and/or accidental release of pesticides.

**How could the data impact the Agency's future decision-making?**

If monitoring of the chemical is required or performed, the Agency could be able to determine if the chemical is present in the environment at concentrations that are threatening to wildlife (or to humans, in the case of drinking waters), according to the levels of concern (LOCs). If that is the case, measures to prevent these concentrations to occur could be taken. The data could also be used by enforcement entities like the states or government agencies or departments. Without these data, the potential for the determination of residues of tralomethrin and deltamethrin in soil, water and sediment is restricted. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for tralomethrin which may otherwise be avoided, or which are unnecessarily severe.

**Guideline Number: 850-2100**

**Study Title: Passerine Acute Avian Oral**

**Rationale for Requiring the Data**

Although an acute avian oral studies were received for tralomethrin and the degradate deltamethrin, the Agency updated its data requirements in 40 CFR Part 158 (October 26, 2007) to include an acute oral toxicity study for both a passerine species and either a waterfowl or an upland game species. Prior to starting toxicity testing, a protocol will need to be provided for review.

- Many passerine species utilize agricultural fields, forests, residential areas and surrounding areas, and, therefore, have the potential to be exposed to pesticides used in agricultural, forest, and residential settings
  - It is likely that, for most pesticide use patterns, passerines are more likely to be exposed to pesticides than upland game species and waterfowl
- Passerines are smaller and have faster metabolisms than the waterfowl and upland game bird species traditionally used in avian toxicity tests which could impact their sensitivity to chemicals.

**Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

Since this is a new requirement, EPA was using the results from the toxicity tests for the waterfowl and the upland game bird.

**How will the data be used?**

Data from passerine toxicity studies will be used to estimate potential risks to birds associated with uses of tralomethrin and the degradate deltamethrin. The data will reduce uncertainties associated with the current risk assessment for passerine species and will improve our understanding of the potential effects of tralomethrin and deltamethrin.

**How could the data impact the Agency's future decision-making?**

Because birds significantly contribute to overall environmental quality, a solid understanding of the potential risks to birds, including passerine species, is essential for sound environmental management. Without acceptable data for tralomethrin and the degradate deltamethrin, the Agency cannot determine the levels of tralomethrin and deltamethrin that result in effects to passerine species. If the data indicates that registered tralomethrin usage may pose a risk of adverse effects to non-target birds above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for tralomethrin which may otherwise be avoided, or which are unnecessarily severe.

**Guideline Number: 850.1075**

**Study Title: Fish Acute Toxicity (saltwater, tralomethrin TEP only)**

**Guideline Number: 850.1025**

**Study Title: Oyster Acute Toxicity (saltwater, tralomethrin TEP only)**

**Guideline Number: 850.1035**

**Study Title: Mysid Acute Toxicity (saltwater, tralomethrin TEP only)**

#### **Rationale for Requiring the Data**

Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas and the expected environmental concentrations in aquatic environments reported in previous tralomethrin assessments. Tralomethrin technical is highly toxic to estuarine/marine fish and invertebrates on an acute basis, but no information has been submitted for the tralomethrin TEP. A new study is required based on the absence of acceptable data to satisfy the guidelines for acute estuarine/marine fish and invertebrate studies with the typical end-use product.

#### **Practical Utility of the Data**

##### **How did the Agency make its re-registration decision without this data?**

To address potential risks, the Agency imposed mitigation, as an interim measure, which included reduced use rates and application restrictions.

##### **How will the data be used?**

These data are needed for a registration review decision and for an endangered species assessment, which will be conducted as part of that decision. The data would allow the Agency to determine acute and chronic risk to estuarine/marine organisms from exposure to tralomethrin. The effects data would be used to determine the likelihood that exposure to tralomethrin can potentially impact aquatic communities, either by direct effects or by indirect effects on other organisms by reducing their food sources. Additionally, endpoints may be used to estimate chronic toxicity to other estuarine/marine organisms with acute toxicity data using an acute-to-chronic ratio.

##### **How could the data impact the Agency's future decision-making?**

If future endangered species risk assessments are performed without these data, the Agency would have to assume that the tralomethrin "may affect" endangered estuarine/marine organisms directly (and endangered species from other taxa indirectly), and use of tralomethrin might need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin which are unnecessarily severe.

**Guideline Number: 850.1450**

**Study Title: Fish Early Life-Stage (saltwater)**

**Guideline Number: 850.1500**

**Study Title: Fish Life Cycle (saltwater)**

#### **Rationale for Requiring the Data**

Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas. Both tralomethrin and deltamethrin are highly toxic to estuarine/marine fish on an acute basis. A study is required based on the absence of acceptable data to satisfy the guideline for an early life stage estuarine/marine fish study.

Chronic studies on estuarine/marine organisms are required to support uses by which significant concentrations of a chemical are expected to enter into estuarine/marine environments. Persistence in water (e.g., half-life in water >4 days) can also trigger this data requirement.

#### **Practical Utility of the Data**

##### **How did the Agency make its re-registration decision without these data?**

The previous assessment provided for a conditional registration while waiting for acceptable data to be reviewed.

##### **How will the data be used?**

The data would allow the Agency to determine chronic effects, including effects on reproductive success and growth, to estuarine/marine fish from water column exposure to tralomethrin and the degradate deltamethrin. The effects data would be used to determine the likelihood that the chronic risks can potentially impact aquatic communities, either by direct effects on fish or by indirect effects on other organisms by reducing their food sources.

##### **How could the data change the Agency's decision, or impact the Agency's future decision-making?**

By conducting a chronic aquatic risk assessment, the Agency would be able to determine the potential risk to nontarget organisms. For endangered species risk assessments performed without these data, the Agency would have to assume that tralomethrin and deltamethrin "may affect" endangered fish directly (and endangered species from other taxa indirectly), and use of tralomethrin might need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin which are unnecessarily severe.

**Guideline Number: 850.1350**

**Study Title: Aquatic Invertebrate Life-Cycle (saltwater, deltamethrin only)**

**Rationale for Requiring the Data**

The acute toxicity of the degradate deltamethrin to estuarine/marine invertebrates indicates the potential for chronic risk to animals in this taxon, and the potential for chronic exposure exists. Tralomethrin has the potential to enter estuarine/marine water bodies based on current usage patterns that include coastal areas. The parent compound tralomethrin exhibits chronic toxicity effects to estuarine/marine invertebrates. Without this study, the Agency would have to presume chronic risk to listed and non-listed estuarine/marine invertebrates, but would not be able to quantify the risk.

The Agency had conditionally required fish early-life stage and aquatic invertebrate life-cycle studies (guidelines 850.1300, 850.1350, and 850.1400) for terrestrial food and nonfood, aquatic food and nonfood, forestry, and domestic outdoor uses.

**Practical Utility of the Data**

**How did the Agency make its re-registration decision without this data?**

To address potential risks, the Agency imposed mitigation, as an interim measure, which included reduced use rates and application restrictions.

**How will the data be used?**

The aquatic invertebrate life-cycle study would allow the Agency to analyze chronic effects, including effects on reproductive success and growth, to saltwater invertebrates. The effects data would be used to determine the likelihood that the chronic risks can potentially impact aquatic communities, either by direct effects on invertebrates or by indirect effects on fish by reducing their food sources. By refining the assessment, the Agency would be able to determine whether the mitigation imposed as part of the reregistration process was appropriate for tralomethrin due to toxicity concerns with the degradate deltamethrin.

**How could the data impact the Agency's future decision-making?**

If future endangered species risk assessments are performed without these data, the Agency would have to assume that the degradate deltamethrin "may affect" endangered invertebrates directly (and endangered species from other taxa indirectly), and use of tralomethrin might need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin which are unnecessarily severe.

**Guideline Number: None**

**Study Title: Whole sediment: Chronic invertebrates freshwater and marine**

**Rationale for Requiring the Data**

No chronic sediment toxicity tests for freshwater or marine invertebrates have been submitted to satisfy the Agency's updated data requirements for outdoor uses in 40 CFR Part 158 (October 26, 2007) for tralomethrin or deltamethrin. For sediment studies involving pyrethroids, tests on *Hyaella azteca*, *Chironomus tentans*, and *Leptocheirus plumulosus* are requested. Although both are freshwater species, *Hyaella* and *Chironomus* differ substantially in their ecological niche (i.e., epibenthic vs. infaunal species), physiology, and there is some evidence suggesting *Hyaella* is among the more sensitive invertebrates to some pyrethroids based on water column tests (Anderson et al. 2006).

- Benthic organisms inhabit sediment environments that may be exposed to run-off or spray drift from tralomethrin applications used in agricultural, forest, and residential settings
- Previous studies have identified a potential adverse effect for freshwater and estuarine/marine aquatic organisms based on water column toxicity values. Therefore, there is uncertainty associated with that estimate that can be reduced using data from a toxicity test with benthic organisms.
- There is the potential for persistent exposure from tralomethrin and deltamethrin in sediment indicated by the fate properties and open literature studies on pyrethroids (Stout II, et al. 2009, Weston et al. 2005, and Amweg et al. 2006).

**Practical Utility of the Data**

**How did the Agency make its registration decision without these data?**

Surface waters EECs were estimated, while the benthic zone of the bodies of water could not be estimated at the time. The possibility of accumulation of the chemical in sediments was stressed in all the reviews. It was noted that LOCs for aquatic organisms were exceeded using a variety of methods to calculate EECs. Recently, the Agency has used the pore water EECs, generated by PRZM/ EXAMS, for other synthetic pyrethroids with similar aquatic toxicity and level of binding to soils/ sediments than tralomethrin and deltamethrin. Using the equilibrium partitioning theory (EqP), the RQs were estimated for other pyrethroids. It has been found that the RQs exceeded the LOCs for these chemicals. A similar finding is expected for tralomethrin and deltamethrin.

**How will the data be used?**

Data from sediment toxicity studies will be used to estimate potential risks to benthic organisms associated with uses of tralomethrin and the degradate deltamethrin. The data will reduce uncertainties associated with the current risk assessment for benthic species and will improve our understanding of the potential effects of deltamethrin.

**How could the data impact the Agency's future decision-making?**

Although there was uncertainty in estimating the effect of tralomethrin & deltamethrin on benthic organisms in the previous assessment, there was a potential risk associated with adverse effects identified for estuarine/marine acute and chronic organisms. Acceptable data for benthic organisms will reduce the uncertainty from the previous assessment. If the data indicates that registered tralomethrin usage may pose a risk of adverse effects to non-target benthic organisms

above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for tralomethrin which may otherwise be avoided, or which are unnecessarily severe.

**Guideline Numbers: 850.4150 and 850.4250**

**Study Title: Vegetative vigor and Seedling emergence, Tier I/ Tier II**

**Rationale for Requiring the Data**

No acceptable toxicity data are currently available to assess the risk of tralomethrin and the degradate deltamethrin to terrestrial plants.

Since tralomethrin has residential outdoor uses, vegetative vigor and seedling emergence studies are required. These phytotoxicity data are needed to evaluate the level of pesticide exposure to non-target terrestrial and aquatic plants and to assess the impact of pesticides on endangered and threatened plants.

**Practical Utility of the Data**

**How did the Agency make its re-registration decision without these data?**

Since EPA was unable to evaluate the potential risks to terrestrial plants associated with the proposed uses of tralomethrin, risks were not precluded for vegetative vigor and seedling emergence endpoints for terrestrial plants.

**How will the data be used?**

Data from terrestrial plant toxicity studies will be used to estimate potential risks to plants associated with uses of tralomethrin and the degradate deltamethrin. The data will reduce uncertainties associated with the current risk assessment for terrestrial plants and will improve our understanding of the potential effects of tralomethrin and deltamethrin on plants.

**How could the data impact the Agency's future decision-making?**

Because plants form the basis of most habitats and significantly contribute to overall environmental quality, a solid understanding of the potential risks to terrestrial plants is essential for sound environmental management. Without acceptable plant growth data for tralomethrin and deltamethrin, the Agency cannot determine the levels of tralomethrin that result in effects to terrestrial plants. If the data indicates that registered tralomethrin usage may pose a risk of adverse effects to non-target terrestrial plants above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for tralomethrin which may otherwise be avoided, or which are unnecessarily severe.

**Guideline Number: 850.4400**

**Study Title: Aquatic Vascular Plant Growth-*Lemna* spp. Tiers I/II**

#### **Rationale for Requiring the Data**

No acceptable studies for tralomethrin and the degradate deltamethrin have been submitted for vascular aquatic plants. The Agency has finalized its update to the data requirements in 40 CFR Part 158. In these updated data requirements, which were promulgated on October 26, 2007, vascular plant testing is required for pesticides such as tralomethrin with outdoor uses.

#### **Practical Utility of the Data**

**How did the Agency make its re-registration decision without these data?**

Since EPA was unable to evaluate the potential risks to aquatic vascular plants associated with the use of tralomethrin, risks were presumed for vascular aquatic plants.

**How will the data be used?**

Data from aquatic plant toxicity studies will be used to estimate potential risks to plants associated with uses of tralomethrin and the degradate deltamethrin. The data will reduce uncertainties associated with the current risk assessment for aquatic plants and will improve our understanding of the potential effects of tralomethrin on vascular aquatic plants.

**How could the data change the Agency's decision, or impact the Agency's future decision-making?**

Because plants form the basis of most habitats and significantly contribute to overall environmental quality, a solid understanding of the potential risks to aquatic plants is essential for sound environmental management. Without plant growth data for tralomethrin, the Agency cannot determine the levels of tralomethrin and the degradate deltamethrin that result in effects to vascular aquatic plants. If the data indicates that registered tralomethrin usage may pose a risk of adverse effects to non-target aquatic vascular plants above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk.

If future endangered species risk assessments are performed without these data, the Agency would have to assume that tralomethrin "may affect" endangered plants and use of tralomethrin might need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for tralomethrin that may be unnecessarily severe.

**Guideline Number: 850.5400**

**Study Title: Algal toxicity test, Tier I/II**

**Rationale for Requiring the Data**

No toxicity data are currently available to assess the risk of tralomethrin and the degradate deltamethrin to aquatic nonvascular plants. Since tralomethrin has residential outdoor uses, Tier I/II aquatic nonvascular plant studies are required. These phytotoxicity data are needed to evaluate the level of pesticide exposure to non-target aquatic plants and to assess the impact of pesticides on endangered and threatened plants.

**Practical Utility of the Data**

**How did the Agency make its re-registration decision without these data?**

Since EPA was unable to evaluate the potential risks to aquatic nonvascular plants associated with the proposed uses of tralomethrin, risks were presumed for aquatic plants.

**How will the data be used?**

Data from Tier I/II nonvascular aquatic plant toxicity studies will be used to estimate potential risks to plants associated with uses of tralomethrin. The data will reduce uncertainties associated with the current risk assessment for nonvascular aquatic plants and will improve our understanding of the potential effects of tralomethrin and the degradate deltamethrin.

**How could the data impact the Agency's future decision-making?**

Because plants form the basis of most habitats and significantly contribute to overall environmental quality, a solid understanding of the potential risks to nonvascular aquatic plants is essential for sound environmental management. Without plant growth data for tralomethrin and the degradate deltamethrin, the Agency cannot determine the levels of tralomethrin that result in effects to aquatic plants. If the data indicates that registered tralomethrin usage may pose a risk of adverse effects to non-target aquatic nonvascular plants above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for tralomethrin which may otherwise be avoided, or which are unnecessarily severe.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**MEMORANDUM**

Date: 3/4/2010

SUBJECT: Acephate. Review of Metabolism Study in Rats (MRID No. 46366201)

PC Code: 103301

Decision No.: NA

Petition No.: NA

Risk Assessment Type: NA

TXR No.: 0052925

MRID No.: 46366201

DP Barcode: D310317

Registration No.: NA

Regulatory Action: NA

Case No.: NA

CAS No.: 30560-19-1

40 CFR: NA

FROM: Paul Chin, Ph.D. *Paul Chin*  
Risk Assessment Branch VII  
Health Effects Division (7509P)  
Office of Pesticide Programs

THROUGH: Linda Taylor, Ph.D. *Linda Taylor*  
Michael S. Metzger, Chief  
Risk Assessment Branch VII  
Health Effects Division (7509P)  
Office of Pesticide Programs

TO: Susan Bartow, CRM  
Pesticide Re-evaluation Division (7508P)  
Office of Pesticide Programs

**I. CONCLUSIONS**

The registrant, Valent U.S.A. Corporation, submitted a metabolism study in rats. This study was reviewed in HED and was classified **Acceptable/Guideline**. The DER for this study is attached to this memorandum and the citation and the conclusion of this study are presented below.

## II. & III. ACTION REQUESTED and BACKGROUND

The registrant, Valent U.S.A. Corporation, submitted this study. PRD requested RAB VII, HED to review and prepare DER for this study.

## IV. REVIEW SUMMARY

**CITATION:** Johnson, T. L. (2004). An Oral (Gavage) Metabolism and Toxicokinetic Study with  $^{14}\text{C}$ -Acephate in Rats. WIL Research Laboratories, Inc. Project Number: WIL/476002, 200400302. July 23, 2004. MRID No. 46366201. Unpublished

**EXECUTIVE SUMMARY:** In a rat metabolism study (MRID 46366201),  $^{14}\text{C}$ -S-methyl-labeled acephate ( $^{14}\text{C}$ -acephate; product # 516; lot # 000619; purity >95% a.i) in water was administered by oral gavage to Sprague-Dawley Crl:CD (SD)IGS BR rats (3 or 4 rats/sex/dose) at dose levels of 25 or 100 mg/kg. In the first phase of the study (Toxicokinetic Phase), two dose groups (Groups 1 and 2; each with 2 sub-groups) consisting of 6 animals per gender were treated with single doses at 25 or 100 mg/kg. Blood samples were collected from both dose groups of rats following dosing (Subgroup A: 0.5, 2, 8, 48, and 96 hours; Subgroup B: 1, 4, 24, 72, 168 hours), and the plasma was isolated. The toxicokinetic data obtained from Groups 1 and 2 were used to establish the time points for determination of tissue distribution in the second phase. The plasma concentrations of radioactivity were determined at various time points up to 168 hours post dosing, and the toxicokinetic (TK) parameters were calculated from the plasma concentration versus time curves.

In the second phase of the study (Metabolism Phase), two dose groups (Groups 3 and 4) consisting of 4 animals per gender were treated with single doses at 25 or 100 mg/kg per time point (0.5, 1, 2, 8, and 24 hours). The concentrations of radioactivity in tissues and excreta were determined, and metabolites in the urine were identified and quantified. The 24-hour animals were used to provide excreta for metabolite profiling and mass balance.

Tissue concentrations appeared to be dose proportional and exhibited no gender differences; no differences in absorption or excretion were observed between the sexes and dose levels; there were no gender differences at either dose level with respect to TK parameters, which were proportional to dose.

Acephate was absorbed rapidly by rats of both sexes as the time point of maximum plasma concentration ( $T_{\max}$ ) was observed 0.5 hours after dosing with 25 and 100 mg/kg. After having reached peak levels, plasma concentrations declined continuously. Following an acute oral dose of 25 mg/kg, both the  $C_{\max}$  values (21.9 and 24.9  $\mu\text{g/g}$ ) and  $\text{AUC}_{0-168}$  values (148 and 150  $\mu\text{g-h/g}$ ) were similar for males and females, respectively. The elimination rate constant values were 0.014 and 0.012  $\text{h}^{-1}$  and the terminal phase half-lives were 50 and 58 hours for males and females, respectively, demonstrated similarity between the sexes.

Following an acute oral dose of 100 mg/kg,  $C_{\max}$  values were 84 and 98  $\mu\text{g/g}$  and  $\text{AUC}_{0-168}$  values were 576 and 545  $\mu\text{g-h/g}$  for males and females, respectively. The elimination rate

constant values were 0.014 and 0.13 h<sup>-1</sup> and the terminal phase half-lives were 49 and 52 hours for males and females, respectively, demonstrating similarity between the sexes.

Total recoveries of radioactivity ranged from 103.4-105.6% and 97.3-98.0% of the administered dose following an oral dose of 25 and 100 mg/kg, respectively, with no differences observed between sexes and dose levels. In the 25 mg/kg animals, the urine, feces and expired carbon dioxide accounted for 86.1%, 2.3% and 9.5% of the administered dose in males and 88.9%, 2.4% and 9.7% of the administered dose in females, respectively. In the 100 mg/kg animals, the urine, feces and carbon dioxide accounted for 82.7%, 3.0% and 5.7% of the administered dose in the males and 87%, 1.8% and 4.6% of the administered dose in the females, respectively. In the 25 and 100 mg/kg animals, cage wash, tissues, GI tract and carcass each account for <3.3% of the administered dose.

The highest concentrations of radioactivity were found in tissues at 0.5 h or 1 h after administration at 25 and 100 mg/kg. Tissues concentration of acephate decreased, generally, by an order of magnitude or more by 24-h post-dosing. The highest concentrations of radioactivity (in terms of  $\mu\text{g}$  equivalents/g tissue) in the 25 and 100 mg/kg groups at 24-h post-dosing were found in liver (2.54-7.87), kidney (2.40-6.28), lung (2.10-6.19), spleen (2.14-7.55), bone (1.4-5.55), GI tract (2.59-7.93), adrenal glands (2.86-11.98) and GI tract contents (1.36-17.69). Overall, tissue concentrations appeared to be dose proportional and exhibited no gender differences. At 24-h post-dosing, the highest levels of radioactivity (in terms of % of the administered dose) were found in liver (0.27-0.47%), GI tract (0.28-0.52%) and GI tract contents (0.18-0.69%). All other tissues contained less than 0.1% of the administered dose.

Based on the TLC analyses of urine samples collected at 6, 12, and 24 h post-dosing of <sup>14</sup>C-acephate at 25 or 100 mg/kg, there was no difference in the metabolic profile of urine between sexes and dose levels. The major radioactive component in urine from rats dosed with <sup>14</sup>C-acephate at 25 and 100 mg/kg was unmetabolized acephate (77-80% of dose; approximately 90% of radioactivity in urine sample). The only significant metabolism of acephate is the formation of <sup>14</sup>CO<sub>2</sub> (9-10% of dose). Small quantities of methamidophos (4% of dose) and 3 unknown components (<4% of dose) were found in the urine. The unknown components were des-acetamidoacephate (DMPT), 0-desmethyl acephate (SMPT), and 0-desmethyl methamidophos (SMPAA). However, metabolic origins of methamidophos and these 3 metabolites are uncertain because they were present as contaminants in the dosing solutions at about the same percentage.

This metabolism study is classified **acceptable/guideline** and satisfies the guideline requirements for a metabolism study [OPPTS 870.7485, OECD 417] in rats.



**EPA Reviewer:** Paul Chin, Ph.D.  
**Risk Assessment Branch VII, Health Effects Division (7509P)**  
**EPA Secondary Reviewer:** Linda Taylor, Ph.D.  
**Risk Assessment Branch VII, Health Effects Division (7509P)**

**Signature:** Paul Chin  
**Date:** 2/23/2010  
**Signature:** Linda Taylor  
**Date:** 2/24/2010

**TXR#:** 0052925

<b>DATA EVALUATION RECORD</b>
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**STUDY TYPE:** Metabolism - rat; OPPTS 870.7485 [§85-1]; OECD 417

**DP BARCODE:** D310317

**P.C. CODE:** 103301

**MRID No.:** 46366201

**TEST MATERIAL (RADIOCHEMICAL PURITY):**  $^{14}\text{C}$ -S-methyl-labeled acephate ( $^{14}\text{C}$ -acephate; purity >95% a.i)

**SYNONYMS:** ORTHENE® Technical; 0, S-Dimethyl acetylphosphoramidothioate

**CITATION:** Johnson, T. L. (2004). An Oral (Gavage) Metabolism and Toxicokinetic Study with  $^{14}\text{C}$ -Acephate in Rats. WIL Research Laboratories, Inc. Project Number: WIL/476002, 200400302. July 23, 2004. MRID No. 46366201. Unpublished

**SPONSOR:** Valent U.S.A. Corporation

**EXECUTIVE SUMMARY:** In a rat metabolism study (MRID 46366201),  $^{14}\text{C}$ -S-methyl-labeled acephate ( $^{14}\text{C}$ -acephate; product # 516; lot # 000619; purity >95% a.i) in water was administered by oral gavage to Sprague-Dawley CrI:CD (SD)IGS BR rats (3 or 4 rats/sex/dose) at dose levels of 25 or 100 mg/kg. In the first phase of the study (Toxicokinetic Phase), two dose groups (Groups 1 and 2; each with 2 sub-groups) consisting of 6 animals per gender were treated with single doses at 25 or 100 mg/kg. Blood samples were collected from both dose groups of rats following dosing (Subgroup A: 0.5, 2, 8, 48, and 96 hours; Subgroup B: 1, 4, 24, 72, 168 hours), and the plasma was isolated. The toxicokinetic data obtained from Groups 1 and 2 were used to establish the time points for determination of tissue distribution in the second phase. The plasma concentrations of radioactivity were determined at various time points up to 168 hours post dosing, and the toxicokinetic (TK) parameters were calculated from the plasma concentration versus time curves.

In the second phase of the study (Metabolism Phase), two dose groups (Groups 3 and 4) consisting of 4 animals per gender were treated with single doses at 25 or 100 mg/kg per time point (0.5, 1, 2, 8, and 24 hours). The concentrations of radioactivity in tissues and excreta were

determined, and metabolites in the urine were identified and quantified. The 24-hour animals were used to provide excreta for metabolite profiling and mass balance.

Tissue concentrations appeared to be dose proportional and exhibited no gender differences; no differences in absorption or excretion were observed between the sexes and dose levels; there were no gender differences at either dose level with respect to TK parameters, which were proportional to dose.

Acephate was absorbed rapidly by rats of both sexes as the time point of maximum plasma concentration ( $T_{max}$ ) was observed 0.5 hours after dosing with 25 and 100 mg/kg. After having reached peak levels, plasma concentrations declined continuously. Following an acute oral dose of 25 mg/kg, both the  $C_{max}$  values (21.9 and 24.9  $\mu\text{g/g}$ ) and  $AUC_{0-168}$  values (148 and 150  $\mu\text{g}\cdot\text{h/g}$ ) were similar for males and females, respectively. The elimination rate constant values were 0.014 and 0.012  $\text{h}^{-1}$  and the terminal phase half-lives were 50 and 58 hours for males and females, respectively, demonstrated similarity between the sexes.

Following an acute oral dose of 100 mg/kg,  $C_{max}$  values were 84 and 98  $\mu\text{g/g}$  and  $AUC_{0-168}$  values were 576 and 545  $\mu\text{g}\cdot\text{h/g}$  for males and females, respectively. The elimination rate constant values were 0.014 and 0.13  $\text{h}^{-1}$  and the terminal phase half-lives were 49 and 52 hours for males and females, respectively, demonstrating similarity between the sexes.

Total recoveries of radioactivity ranged from 103.4-105.6% and 97.3-98.0% of the administered dose following an oral dose of 25 and 100 mg/kg, respectively, with no differences observed between sexes and dose levels. In the 25 mg/kg animals, the urine, feces and expired carbon dioxide accounted for 86.1%, 2.3% and 9.5% of the administered dose in males and 88.9%, 2.4% and 9.7% of the administered dose in females, respectively. In the 100 mg/kg animals, the urine, feces and carbon dioxide accounted for 82.7%, 3.0% and 5.7% of the administered dose in the males and 87%, 1.8% and 4.6% of the administered dose in the females, respectively. In the 25 and 100 mg/kg animals, cage wash, tissues, GI tract and carcass each account for <3.3% of the administered dose.

The highest concentrations of radioactivity were found in tissues at 0.5 h or 1 h after administration at 25 and 100 mg/kg. Tissues concentration of acephate decreased, generally, by an order of magnitude or more by 24-h post-dosing. The highest concentrations of radioactivity (in terms of  $\mu\text{g}$  equivalents/g tissue) in the 25 and 100 mg/kg groups at 24-h post-dosing were found in liver (2.54-7.87), kidney (2.40-6.28), lung (2.10-6.19), spleen (2.14-7.55), bone (1.4-5.55), GI tract (2.59-7.93), adrenal glands (2.86-11.98) and GI tract contents (1.36-17.69). Overall, tissue concentrations appeared to be dose proportional and exhibited no gender differences. At 24-h post-dosing, the highest levels of radioactivity (in terms of % of the administered dose) were found in liver (0.27-0.47%), GI tract (0.28-0.52%) and GI tract contents (0.18-0.69%). All other tissues contained less than 0.1% of the administered dose.

Based on the TLC analyses of urine samples collected at 6, 12, and 24 h post-dosing of  $^{14}\text{C}$ -acephate at 25 or 100 mg/kg, there was no difference in the metabolic profile of urine between sexes and dose levels. The major radioactive component in urine from rats dosed with  $^{14}\text{C}$ -

**3. Test animals:**

<b>Species:</b>	Rat		
<b>Strain:</b>	Sprague-Dawley Crl:CD (SD)IGS BR		
<b>Age/range of weight at 1-2 days prior to dosing</b>	Approximately 7-9 weeks; males 224-314 g Approximately 9-11 weeks; females 190-274 g 192-286 g pp35-36		
<b>Source:</b>	Charles River Laboratories (Raleigh, NC)		
<b>Housing:</b>	Steel wire mesh cages (1 animal/cage)		
<b>Feed and Water:</b>	Animals were provided Certified Meal LabDiet® 5002. Feed and municipal water was provided <i>ad libitum</i> .		
<b>Environmental conditions:</b>	Temperature:	20-22°C	
	Humidity:	36-65%	
	Air changes:	10 changes/hour	
	Photoperiod:	12 hours dark/12 hours light	
<b>Acclimation period:</b>	Approximately 7-10 days		

**4. Preparation of test substance:**

The dosing formulation for Groups 1 (25 mg/kg) and 2 (100 mg/kg) were prepared by combining 2.8 mg of the radiolabeled test substance with 0.0972 g and 0.3972 g of unlabeled acephate in a bottle calibrated at 40 mL, respectively. Deionized water was then added to the bottle to the calibration mark.

Prior to preparation of the dosing solution for Group 3, a stock solution of the radiolabeled acephate was prepared by dissolving the test article in 2 mL of methanol. This produced a radiolabeled stock solution with a concentration of 40.4 mg/mL. For Group 3 (25 mg/kg), Sub-groups 1-4, the dosing formulation was prepared by placing 158 µL of the radiolabeled stock solution with 0.2361 g of unlabeled acephate in a bottle calibrated at 97 mL and evaporating the solvent to near dryness. The dosing formulation for Group 3, Sub-group 5 was prepared by combining 209 µL of the radiolabeled stock solution with 0.0716 g of unlabeled acephate in a bottle calibrated at 32 mL and evaporating the solvent to near dryness.

Prior to preparation of the dosing solution for Group 4, a stock solution of the radiolabeled acephate was prepared by dissolving the test article in deionized water. This produced a radiolabeled stock solution with a concentration of 0.54 mg/mL. For Group 4 (100 mg/kg), Sub-groups 1-4, the dosing formulation was prepared by combining 13.158 mL of the radiolabeled stock solution with 1.0729 g of unlabeled acephate in a bottle calibrated at 108 mL. The dosing formulation for Group 4, Sub-group 5 was prepared by combining 15.595 mL of the radiolabeled stock solution with 0.3116 g of unlabeled acephate in a bottle calibrated at 32 mL.

acephate at 25 and 100 mg/kg was unmetabolized acephate (77-80% of dose; approximately 90% of radioactivity in urine sample). The only significant metabolism of acephate is the formation of  $^{14}\text{CO}_2$  (9-10% of dose). Small quantities of methamidophos (4% of dose) and 3 unknown components (<4% of dose) were found in the urine. The unknown components were des-acetamidoacephate (DMPT), 0-desmethyl acephate (SMPT), and 0-desmethyl methamidophos (SMPAA). However, metabolic origins of methamidophos and these 3 metabolites are uncertain because they were present as contaminants in the dosing solutions at about the same percentage.

This metabolism study is classified **acceptable/guideline** and satisfies the guideline requirements for a metabolism study [OPPTS 870.7485, OECD 417] in rats.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

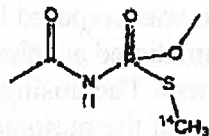
## I. MATERIALS AND METHODS

### A. MATERIALS:

#### 1a. Radiolabeled Test Compound:

<b>Radiolabeled Test Material:</b>	$^{14}\text{C}$ -S-methyl-Acephate
<b>Radiochemical purity</b>	>95%
<b>Specific Activity</b>	40-60 mCi/mM
<b>Description</b>	Not provided
<b>Product #/Lot #</b>	516/000619

Position of  $^{14}\text{C}$  label in  $^{14}\text{C}$ -S-methyl-acephate is shown below:



#### 1b. Non-radiolabeled Test Compound:

<b>Non-Radiolabeled Test Material:</b>	Acephate
<b>Description:</b>	Not provided
<b>Product #/Lot #</b>	1027/T3-352-01-02AFT
<b>Purity:</b>	99.1%
<b>CAS #</b>	30560-19-1

#### 2. Vehicle for oral dosing: deionized water

**Stability, homogeneity, and concentration analyses of the test substance preparations:**

**Stability:** The pre- and post-dosing radiopurity values (>95%) indicated stability of the radiolabeled compound over the time course of dosing.

**Homogeneity (% CV):** <6.5% based on the analyses of sample preparations for all Groups. The formulations were considered homogeneous as indicated by the low coefficients of variations.

**Concentration (% of nominal):** Not reported

**B. STUDY DESIGN AND METHODS**

This study was designed to determine the toxicokinetics, absorption, distribution, elimination and metabolism of acephate in the rat.

**Study dates:** In-Life: start July 29, 2003; end: June 1, 2004

In the First phase of the study (Toxicokinetic Phase), two dose groups (Groups 1 and 2) consisting of six animals per gender were treated at a target dosage level of 25 or 100 mg/kg (about 10% of the LD50 in rats). Blood samples were collected from both groups of animals at specified times following dosing.

In the Second phase of the study (Metabolism Phase), two dose groups (Groups 3 and 4) consisting of four animals per gender per subgroup were treated at a target dosage level of 25 or 100 mg/kg. The two dose groups were divided into five sub-groups based on their scheduled time of euthanasia: 0.5, 1, 2, 8, and 24 h post-dosing. In addition to tissue distribution, the animals in the 24-h group were used to provide excreta for metabolite profiling and mass balance.

1. **Group Arrangements:** Animals were assigned randomly to the four test groups as noted below.

**Dosing Groups and Study Design**

Dosing Groups	Dosage Level	Dosage volume	Sub-group	No. of animals	Time of blood collection (hour)
1	25 mg/kg	10 ml/kg	A	3M, 3F	0.5, 2, 8, 48, 96
			B	3M, 3F	1, 4, 24, 72, 168
2	100 mg/kg	10 ml/kg	A	3M, 3F	0.5, 2, 8, 48, 96
			B	3M, 3F	1, 4, 24, 72, 168
					<b>Time of euthanasia (post-dosing: hour)</b>
3	25 mg/kg	10 ml/kg	1	4M, 4F	0.5
			2	4M, 4F	1
			3	4M, 4F	2
			4	4M, 4F	8
			5	4M, 4F	24
4	100 mg/kg	10 ml/kg	1	4M, 4F	0.5
			2	4M, 4F	1
			3	4M, 4F	2
			4	4M, 4F	8
			5	4M, 4F	24

**2. Dosing and sample collection:**

Acephate formulations were administered orally at a dosage volume of 10 ml/kg by gavage using a syringe and ball-tipped cannula. The dosing syringe was weighed before and after delivery of the dose; the difference in weights was used to calculate the actual administered dose.

**a. Toxicokinetic studies (Dose Groups 1 and 2)**

Blood samples (approximately 0.5 mL) were collected from each animal via a lateral tail vein. The time that blood samples were collected depended on the sub-group assignment as indicated in the above table.

**b. Absorption, distribution, metabolism and excretion (ADME) studies (Dose Groups 3 and 4)**

Urine and feces were collected separately on ice from each animal in sub-group 5 on the following schedule: 0-6, 6-12, and 12-24 h post-dosing. At each collection, the interior surface of the metabolism units was rinsed with deionized water, and the water was retained separately from the urine collection. After the final collection, the metabolism units were further washed with deionized water:methanol (1:1, v:v), and the wash weight was measured and retained as a separate sample for analysis.

Expired air was collected separately from each animal in sub-group 5 on the following schedule: 0-4, 4-8, 8-12, 12-16, 16-20, and 20-24 h post dosing. Expired air from each unit was drawn through a trap containing Carbo-Sorb® E (Packard BioScience Co., Meriden, CT) in order to trap any expired  $^{14}\text{C}\text{O}_2$ .

At 0.5, 1, 2, 8, and 24 h after dose administration, the animals in a sub-group were euthanized by asphyxiation with carbon dioxide inhalation. After euthanasia, each animal was weighed, the abdominal and thoracic cavity opened, and a blood sample collected from the vena cava. Blood samples were collected into tubes containing sodium heparin as the anticoagulant. Plasma and the cellular fraction were separated by centrifugation and retained for analysis of total radioactivity. The following tissues were collected from each animal:

#### **Tissues Collected at Terminal Sacrifice**

Adipose tissue	Kidneys
Adrenal glands	Liver
Bone (femur w/marrow)	Lung
Brain	Muscle
GI tract	Spleen
GI tract contents	Testes
Heart	Thyroid
Uterus/ovaries	

Plasma, urine, cage wash, cage rinse, and expired air samples were mixed with 10 mL of Ultima Gold™ liquid scintillation cocktail for direct analysis by liquid scintillation counter (LSC). Adipose tissue samples were dissolved in Ultima Gold™ liquid scintillation cocktail (Packard Bioscience Co.). The following samples were homogenized and were combusted prior to LSC analysis: lung, testes, kidney, gastrointestinal tract, liver, brain, gastrointestinal tract contents, and fecal samples. Carcass samples were slightly thawed, chopped, refrozen, and ground twice with an electric meat grinder. Heart, spleen, adrenal glands, thyroid glands, muscle, bone, and ovaries/uterus were combusted in entirety prior to LSC analysis.

Radioactivity was determined using a Beckman Model LS 6000TA or ES 6500 liquid scintillation spectrophotometer (Beckman Instruments Inc., Fullerton, CA). Radio-HPLC analyses were performed using a Hitachi HPLC system (Hitachi Ltd., Tokyo, Japan). TLC was used to quantify and identify urinary metabolites of acephate.

Gas Chromatography/Mass Spectrometry (GC/MS) was used to confirm the identity of the test substance prior to its use in the study and to analyze the impurity in the test.

Data for the concentration of acephate equivalents in plasma were subjected to toxicokinetic analysis. The following plasma toxicokinetic parameters were determined: terminal half-life of elimination ( $t_{1/2}$ ), area under the plasma concentration time curves ( $\text{AUC}_{0-t}$ ), maximum

concentration in the plasma ( $C_{\max}$ ), the time ( $t_{\max}$ ) required to reach  $C_{\max}$ , and elimination rate constant ( $K_{el}$ ). The method of calculation is indicated below.

$C_{\max}$	Maximum mean concentration of test material; values empirically determined from data.
$t_{\max}$	Sampling time at which $C_{\max}$ was reached; values empirically determined from data.
$AUC_{0-168} =$	Area under the concentration vs. time curve from 0-168 hours; values were calculated by linear trapezoidal summation using the equation: $AUC_{0-168} = \sum (0.5 \bullet (y_1 + y_2) \bullet \Delta t)$ where $y_1$ and $y_2$ are successive mean concentrations and $\Delta t$ is the sampling interval, in hours, between $y_1$ and $y_2$ .
$AUC_{0-\infty}$	Estimate of the area under the plasma concentration vs. time curve from 0 hour to infinity; values were calculated using the formula: $AUC_{0-\infty} = AUC_{0-168} + (\text{plasma concentration at 168 hr}/K_{el})$ where $AUC_{0-168}$ is defined previously and $K_{el}$ is defined subsequently.
$K_{el}$	Elimination rate constant for the test material in the compartment; values were calculated using the formula: $K_{el} = -\ln [10] \cdot b$ where $b$ is the slope of the least squares linear regression line of the log of mean concentration vs. time over the time interval indicated on the tables.
Half-life	Half-life for the test material in the compartment; values were calculated using the formula: $\text{Half-life} = -\ln [0.5] / K_{el}$ where $K_{el}$ is defined previously.

### **Statistics:**

Radioactivity, in terms of concentration ( $\mu\text{g}$  equivalents/g), was reported for individual samples and as the mean (with  $\pm\text{S.D.}$ ) of animals/dose group.

## **II. RESULTS**

### **Actual doses administered**

The mean actual dose of test substance was 25.2 mg/kg (for both males and females) for Group 3 (sub-groups 1-4) and 24.5-24.9 mg/kg for Group 3 (sub-group 5). The mean actual dose of test substance was 96-97 mg/kg for Group 4 (sub-groups 1-4) and 99-101 mg/kg for Group 4 (sub-group 5).

**A. Toxicokinetic Studies:**

The plasma concentrations of radioactivity and the toxicokinetic parameters after a single oral administration of  $^{14}\text{C}$ -acephate to rats by oral gavage at dose levels of 25 and 100 mg/kg are presented in Table 1. The time point of maximum plasma concentration ( $t_{\max}$ ) was observed 0.5 hours after dosing with 25 and 100 mg/kg. After having reached peak levels, plasma concentrations declined continuously. There was no gender difference at either dose level.

Following an oral dose of 25 mg/kg,  $C_{\max}$  values were 21.9 and 24.9  $\mu\text{g/g}$  and  $\text{AUC}_{0-168}$  values were 148 and 150  $\mu\text{g}\cdot\text{h/g}$  for males and females, respectively. The elimination rate constants were 0.014 and 0.012  $\text{h}^{-1}$  and the terminal phase half-lives were 50 and 58 hours for males and females, respectively.

Following an oral dose of 100 mg/kg,  $C_{\max}$  values were 84 and 98  $\mu\text{g/g}$  and  $\text{AUC}_{0-168}$  values were 576 and 545  $\mu\text{g}\cdot\text{h/g}$  for males and females, respectively. The elimination rate constants were 0.014 and 0.13  $\text{h}^{-1}$  and the terminal phase half-lives were 49 and 52 hours for males and females, respectively.

**B. ADME studies****1. Absorption/Excretion**

No differences in absorption or excretion were observed between the sexes and dose levels. The test compound was absorbed rapidly by rats of both sexes as maximum plasma concentrations were attained within 30 minutes following a single oral dose of acephate at 25 or 100 mg/kg. Percent recovery of the administered dose for animals euthanized at 24 h post-dosing is presented in Table 2 for Group 3 (25 mg/kg) and Group 4 (100 mg/kg) animals. Total recoveries ranged from 103.4-105.6% (Group 3) and 97.3-98.0% (Group 4) of the doses.

In the 25 mg/kg males, the urine, feces and carbon dioxide accounted for 86.1%, 2.3% and 9.5% of the administered dose. In the 25 mg/kg females, the urine, feces and carbon dioxide accounted for 88.9%, 2.4% and 9.7% of the administered dose. In both males and females, cage wash, tissues, GI tract and carcass each account for <3.3% of the administered dose.

In the 100 mg/kg males, the urine, feces and carbon dioxide accounted for 82.7%, 3.0% and 5.7% of the administered dose. In the 100 mg/kg females, the urine, feces and carbon dioxide accounted for 87%, 1.8% and 4.6% of the administered dose. In both males and females, cage wash, tissues, GI tract and carcass each account for <2.4% of the administered dose.

Table 1. Mean plasma concentrations of acephate ( $\mu\text{g}$ equivalent/g) and toxicokinetics values following oral administration at 25 or 100 mg/kg <sup>a</sup>				
Time (h)	25 mg/kg Males N=3	25 mg/kg Females N=3	100 mg/kg Males N=3	100 mg/kg Females N=3
Plasma concentrations of acephate ( $\mu\text{g}$ equivalent/g)				
0.5	21.91 $\pm$ 2.07	24.87 $\pm$ 3.60	83.57 $\pm$ 2.12	98.39 $\pm$ 3.67
1	20.31 $\pm$ 0.32	21.47 $\pm$ 0.80	83.33 $\pm$ 5.07	75.79 $\pm$ 6.02
2	13.96 $\pm$ 1.27	11.91 $\pm$ *	44.32 $\pm$ 6.39	48.72 $\pm$ 2.51
4	4.89 $\pm$ 0.58	5.20 $\pm$ 1.22	18.18 $\pm$ 1.66	16.95 $\pm$ 2.58
8	3.82 $\pm$ 1.05	2.38 $\pm$ 0.73	16.46 $\pm$ 4.23	10.04 $\pm$ 1.50
24	0.68 $\pm$ 0.03	0.96 $\pm$ 0.10	3.03 $\pm$ 0.44	3.11 $\pm$ 0.76
72	0.29 $\pm$ 0.01	0.44 $\pm$ 0.06	1.16 $\pm$ 0.13	1.26 $\pm$ 0.14
168	0.09 $\pm$ 0.00	0.16 $\pm$ 0.02	0.37 $\pm$ 0.04	0.43 $\pm$ 0.03
Toxicokinetics Values				
$C_{\text{max}}$ ( $\mu\text{g/g}$ )	21.9	24.9	83.6	98.4
$t_{\text{max}}$	0.5	0.5	0.5	0.5
$\text{AUC}_{0-168}$ [ $\mu\text{g} \cdot \text{h/g}$ ]	148	150	576	545
$\text{AUC}_{0-\infty}$ [ $\mu\text{g} \cdot \text{h/g}$ ]	155	163	603	578
Elimination rate constant [ $\text{h}^{-1}$ ]	0.0138	0.0119	0.0140	0.0134
Half-life [h]	50.3	58.3	49.4	51.8

a Data were obtained from Tables 1-2 on pages 59-60 of the study report;  
Values represent Means  $\pm$  S. D.

\* N=2 due to insufficient blood sample

TABLE 2. Recovery of radioactivity in tissues and excreta of rats 24 hours after administration of  $^{14}\text{C}$ -acephate at 25 and 100 mg/kg (N=4)

	Cage wash	Tissues	GI tract	Urine	Feces	Carcass	Carbon Dioxide	Total recovery
	% of Dose (Mean $\pm$ SD)							
25 mg/kg Males	0.65 $\pm$ 0.28	1.24 $\pm$ 0.11	0.34 $\pm$ 0.20	86.1 $\pm$ 2.9	2.25 $\pm$ 0.2	3.33 $\pm$ 0.21	9.45 $\pm$ 4.67	103.4 $\pm$ 4.29
25 mg/kg Females	0.65 $\pm$ 0.75	1.07 $\pm$ 0.09	0.28 $\pm$ 0.29	88.9 $\pm$ 1.3	2.36 $\pm$ 0.32	2.63 $\pm$ 0.36	9.69 $\pm$ 1.72	105.6 $\pm$ 1.82
100 mg/kg Males	1.84 $\pm$ 1.00	0.50 $\pm$ 0.09	0.69 $\pm$ 0.94	82.7 $\pm$ 5.6	3.00 $\pm$ 1.03	2.84 $\pm$ 0.97	5.68 $\pm$ 4.28	97.3 $\pm$ 7.43
100 mg/kg Females	1.68 $\pm$ 0.98	0.39 $\pm$ 0.01	0.18 $\pm$ 0.07	87 $\pm$ 2.6	1.77 $\pm$ 0.7	2.43 $\pm$ 0.47	4.56 $\pm$ 1.42	98.0 $\pm$ 1.38

Data were obtained from Tables 4 and 5 on pages 62-63 of MRID 46366201.

### 3. Tissue distribution:

The concentrations of radioactivity in rat tissues/organs at 0.5, 1, 2, 8, and 24 hours after administration of  $^{14}\text{C}$ -acephate at 25 and 100 mg/kg were analyzed. Mean concentrations of radioactivity in tissues (expressed as  $\mu\text{g}$  equivalents/g tissue) at 24-hour post-dose are presented in Table 3. The highest concentrations of radioactivity were found in tissues at 0.5 h or 1 h post-dosing. Tissues concentration of acephate decreased, generally, by an order of magnitude or more by 24-h post-dosing. The highest concentrations of radioactivity (as  $\mu\text{g}$  equivalents/g tissue) in the 25 and 100 mg/kg groups at 24-h post-dosing were found in liver (2.54-7.87), kidney (2.40-6.28), lung (2.10-6.19), spleen (2.14-7.55), bone (1.43-5.55), GI tract (2.59-7.93), adrenal glands (2.86-11.98) and GI tract contents (1.36-17.69). Overall, tissue concentrations appeared to be dose proportional and exhibited no gender differences. At 24-h post-dosing, the highest levels of radioactivity (in terms of % of the administered dose) were found in liver (0.27-0.47%), GI tract (0.28-0.52%) and GI tract contents (0.18-0.69%). All other tissues contained less than 0.1% of the administered dose.

**TABLE 3. Distribution of radioactivity (expressed as  $\mu\text{g}$  equivalents/g tissue) in rat tissues/organs 24 hours after administration of  $^{14}\text{C}$ -acephate at 25 and 100 mg/kg**

	25 mg/kg		100 mg/kg	
	Males	Females	Males	Females
Plasma	$1.15 \pm 0.13$	$1.21 \pm 0.14$	$3.63 \pm 1.49$	$2.60 \pm 0.15$
Red blood cells	$0.73 \pm 0.06$	$0.65 \pm 0.05$	$2.19 \pm 1.13$	$1.23 \pm 0.14$
Liver	$2.74 \pm 0.29$	$2.54 \pm 0.25$	$7.87 \pm 1.40$	$6.89 \pm 0.68$
Kidney	$2.47 \pm 0.25$	$2.40 \pm 0.34$	$6.28 \pm 1.71$	$5.15 \pm 0.68$
Heart	$1.03 \pm 0.08$	$1.01 \pm 0.06$	$3.34 \pm 1.10$	$2.44 \pm 0.19$
Lung	$2.18 \pm 0.48$	$2.10 \pm 0.26$	$6.19 \pm 1.43$	$5.62 \pm 0.61$
Spleen	$2.63 \pm 0.28$	$2.14 \pm 0.32$	$7.55 \pm 1.91$	$4.12 \pm 0.46$
Fat	$0.30 \pm 0.08$	$0.25 \pm 0.15$	$0.89 \pm 0.19$	$0.60 \pm 0.07$
Brain	$0.37 \pm 0.04$	$0.37 \pm 0.06$	$1.65 \pm 0.76$	$1.11 \pm 0.06$
Bone	$1.71 \pm 0.17$	$1.43 \pm 0.10$	$3.48 \pm 1.16$	$5.55 \pm 2.29$
Muscle	$0.65 \pm 0.05$	$0.53 \pm 0.05$	$2.19 \pm 0.78$	$1.50 \pm 0.11$
GI tract	$3.03 \pm 0.83$	$2.59 \pm 0.23$	$7.93 \pm 4.30$	$5.86 \pm 0.54$
Adrenal glands	$3.09 \pm 0.78$	$2.86 \pm 0.72$	$11.58 \pm 2.17$	$11.98 \pm 2.65$
Thyroid	$1.84 \pm 0.46$	$2.34 \pm 0.28$	$5.43 \pm 1.22$	$4.27 \pm 1.08$
Testes/Uterus/Ovaries	$1.04 \pm 0.12$	$3.92 \pm 1.06$	$1.95 \pm 0.61$	$4.47 \pm 1.34$
GI tract contents	$1.56 \pm 0.75$	$1.36 \pm 1.10$	$17.69 \pm 26.74$	$5.39 \pm 2.59$

Data were obtained from Tables 6-23 on pages 64-83 of MRID 46366201

**C. Metabolite characterization studies:**

Table 4 presents the metabolite profile in urine of rats dosed with  $^{14}\text{C}$ -acephate at 25 mg/kg. Based on the TLC analyses of urine samples collected at 6, 12, and 24 h post-dosing of  $^{14}\text{C}$ -acephate at 25 or 100 mg/kg, there was no difference in the metabolic profile of urine between sexes and dose levels. The major radioactive component in urine from rats dosed with  $^{14}\text{C}$ -acephate at 25 and 100 mg/kg was unmetabolized acephate (77-80% of dose; approximately 90% of radioactivity in urine sample). The only significant metabolism of acephate is the formation of  $^{14}\text{CO}_2$  (9-10% of dose). Small quantities of methamidophos (4% of dose) and 3 unknown components (<4% of dose) were found in the urine. The unknown components were **potential**

acephate metabolites des-acetamidoacephate (DMPT), 0-desmethyl acephate (SMPT), and 0-desmethyl methamidophos (SMPAA). However, metabolic origins of methamidophos and these 3 metabolites are uncertain because they were present as contaminants in the dosing solutions at about the same percentage.

Table 4. The metabolite profile in urine of rats dosed with  $^{14}\text{C}$ -acephate at 25 mg/kg

Sampling time (h)	Unknown 1	Unknown 2	Unknown 3	Acephate	Methamidophos
	% of dose	% of dose	% of dose	% of dose	% of dose
<b>Males</b>					
6	0.55 ± 0.37	1.92 ± 0.26	1.12 ± 0.25	55.36 ± 0.46	2.81 ± 0.18
12	0.15 ± 0.17	1.18 ± 0.20	0.16 ± 0.19	15.69 ± 0.44	0.80 ± 0.16
24	0.03 ± 0.06	0.53 ± 0.36	0.07 ± 0.08	5.55 ± 0.54	0.18 ± 0.14
0-24	0.73	3.6	1.4	76.6	3.8
<b>Females</b>					
6	0.79 ± 0.54	2.59 ± 0.51	1.38 ± 0.23	64.62 ± 0.56	2.77 ± 0.31
12	0.05 ± 0.10	1.03 ± 0.58	0.09 ± 0.18	11.50 ± 0.51	0.47 ± 0.03
24	0.05 ± 0.11	0.62 ± 0.10	0.18 ± 0.04	2.57 ± 0.25	0.15 ± 0.18
0-24	1.0	4.2	1.7	78.7	3.4

Data were obtained from Tables 28-29 on pages 88-89 of MRID 46366201

### III. DISCUSSION

#### A. Investigators' conclusions:

The toxicokinetic (TK) phase of the study demonstrated that the TK of acephate equivalents in rat plasma were similar between male and female rats. The TK of acephate in male and female rats dosed at 100 mg/kg was proportional to that of rats dosed at 25 mg/kg. Acephate equivalents were found widely distributed in tissues of male and female rats treated at either 25 or 100 mg/kg acephate. As demonstrated in the TK phase, the highest concentrations were found at 0.5 h or 1 h post-dosing, reflecting the rapid absorption into the bloodstream. The highest concentrations of  $^{14}\text{C}$ -acephate equivalents were found in highly perfused organs such as

kidney, liver and heart. Levels in these tissues were equivalent to the concentration in the plasma at the same intervals. Tissue concentrations of acephate equivalents decreased, generally, by an order of magnitude or more by 24 hours post dose.

Urinary and fecal elimination of acephate equivalents over 24 h post- dosing was similar in both dose groups and both sexes. Low dose group (25 mg/kg) males excreted 86% of the dose in urine while females excreted 89% in urine. High dose group males eliminated 83% of the dose in urine while females excreted 87% in urine. Males and females of both groups eliminated about 2% of the administered dose via the feces. Approximately 9% and 5% of the dose was eliminated as  $^{14}\text{CO}_2$  in the low and high dose group, respectively. Total radioactivity eliminated by animals in the low dose group was 98% of the dose for males and 101% of the dose for females. For the high dose group animals, the total radioactivity eliminated was 92% of the dose for males and 93% of the dose for females.

The results of the TLC analyses of male and female urine samples collected at 6, 12, and 24 h post-dosing showed that nearly 90% of the radioactivity in each animal's urine was unmetabolized acephate regardless of gender or dosage. Methamidophos accounted for about 5% of the radioactivity in the urine. Methamidophos was also present as a contaminant in the dosing solution at about that same percentage; therefore, its metabolic origin is uncertain.

#### **B. Reviewer comments:**

Tissue concentrations appeared to be dose proportional and exhibited no gender differences; no differences in absorption or excretion were observed between the sexes and dose levels; there were no gender differences at either dose level with respect to TK parameters, which were proportional to dose.

Acephate was absorbed rapidly by rats of both sexes as the time point of maximum plasma concentration ( $T_{\max}$ ) was observed 0.5 hours after dosing with 25 and 100 mg/kg. After having reached peak levels, plasma concentrations declined continuously. Following an acute oral dose of 25 mg/kg, both the  $C_{\max}$  values (21.9 and 24.9  $\mu\text{g/g}$ ) and  $\text{AUC}_{0-168}$  values (148 and 150  $\mu\text{g-h/g}$ ) were similar for males and females, respectively. The elimination rate constant values were 0.014 and 0.012  $\text{h}^{-1}$  and the terminal phase half-lives were 50 and 58 hours for males and females, respectively, demonstrated similarity between the sexes.

Following an acute oral dose of 100 mg/kg,  $C_{\max}$  values were 84 and 98  $\mu\text{g/g}$  and  $\text{AUC}_{0-168}$  values were 576 and 545  $\mu\text{g-h/g}$  for males and females, respectively. The elimination rate constant values were 0.014 and 0.13  $\text{h}^{-1}$  and the terminal phase half-lives were 49 and 52 hours for males and females, respectively, demonstrating similarity between the sexes.

Total recoveries of radioactivity ranged from 103.4-105.6% and 97.3-98.0% of the administered dose following an oral dose of 25 and 100 mg/kg, respectively, with no differences observed between sexes and dose levels. In the 25 mg/kg animals, the urine, feces and expired carbon dioxide accounted for 86.1%, 2.3% and 9.5% of the administered dose in males and 88.9%, 2.4% and 9.7% of the administered dose in females, respectively. In the 100 mg/kg animals, the urine,

feces and carbon dioxide accounted for 82.7%, 3.0% and 5.7% of the administered dose in the males and 87%, 1.8% and 4.6% of the administered dose in the females, respectively. In the 25 and 100 mg/kg animals, cage wash, tissues, GI tract and carcass each account for <3.3% of the administered dose.

The highest concentrations of radioactivity were found in tissues at 0.5 h or 1 h after administration at 25 and 100 mg/kg. Tissues concentration of acephate decreased, generally, by an order of magnitude or more by 24-h post-dosing. The highest concentrations of radioactivity (in terms of  $\mu\text{g}$  equivalents/g tissue) in the 25 and 100 mg/kg groups at 24-h post-dosing were found in liver (2.54-7.87), kidney (2.40-6.28), lung (2.10-6.19), spleen (2.14-7.55), bone (1.4-5.55), GI tract (2.59-7.93), adrenal glands (2.86-11.98) and GI tract contents (1.36-17.69). Overall, tissue concentrations appeared to be dose proportional and exhibited no gender differences. At 24-h post-dosing, the highest levels of radioactivity (in terms of % of the administered dose) were found in liver (0.27-0.47%), GI tract (0.28-0.52%) and GI tract contents (0.18-0.69%). All other tissues contained less than 0.1% of the administered dose.

Based on the TLC analyses of urine samples collected at 6, 12, and 24 h post-dosing of  $^{14}\text{C}$ -acephate at 25 or 100 mg/kg, there was no difference in the metabolic profile of urine between sexes and dose levels. The major radioactive component in urine from rats dosed with  $^{14}\text{C}$ -acephate at 25 and 100 mg/kg was unmetabolized acephate (77-80% of dose; approximately 90% of radioactivity in urine sample). The only significant metabolism of acephate is the formation of  $^{14}\text{CO}_2$  (9-10% of dose). Small quantities of methamidophos (4% of dose) and 3 unknown components (<4% of dose) were found in the urine. The unknown components were des-acetamidoacephate (DMPT), 0-desmethyl acephate (SMPT), and 0-desmethyl methamidophos (SMPAA). However, metabolic origins of methamidophos and these 3 metabolites are uncertain because they were present as contaminants in the dosing solutions at about the same percentage.

**C. Study deficiencies:** None that would affect study interpretation.

